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 ********** STN Columbus **********
FILE 'HOME' ENTERED AT 13:20:28 ON 26 SEP 2001
=> file biosis, caba, caplus, embase, japio, lifesci, medline, scisearch, uspatfull
=> e bennettguerrero/au
E1        1   BENNETTEMSLIE G B/AU
E2        3   BENNETTGRAY J/AU
E3        0 --> BENNETTGUERRERO/AU
E4       41   BENNETTGUERRERO E/AU
E5        1   BENNETTI JOHN G/AU
E6        1   BENNETTI S/AU
E7        2   BENNETTIL J R/AU
E8        2   BENNETTJACOBS B/AU
E9        1   BENNETTJOHNSON S/AU
E10       1   BENNETTJONES/AU
E11       4   BENNETTJONES D/AU
E12      14   BENNETTJONES D N/AU
=> s e4
L1       41 "BENNETTGUERRERO E"/AU
=> dup rem l1
PROCESSING COMPLETED FOR L1
L2       41 DUP REM L1 (0 DUPLICATES REMOVED)
=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 41 ANSWERS - CONTINUE? Y/(N):y

L2  ANSWER 1 OF 41  SCISEARCH  COPYRIGHT 2001 ISI (R)
AN  2000:808765  SCISEARCH
GA  The Genuine Article (R) Number: 366LN
TI  Preparation and preclinical evaluation of a novel liposomal complete-core
    lipopolysaccharide vaccine
AU  ***BennettGuerrero E (Reprint)***  ; McIntosh T J; Barclay G R; Snyder D
    S; Gibbs R J; Mythen M G; Poxton I R
CS  COLUMBIA UNIV COLL PHYS & SURG, DEPT ANESTHESIOL, 630 W 168TH ST, NEW
    YORK, NY 10032 (Reprint); DUKE UNIV, DEPT CELL BIOL, DURHAM, NC; UNIV
    EDINBURGH, SCH MED, DEPT MED MICROBIOL, EDINBURGH EH8 9AG, MIDLOTHIAN,
    SCOTLAND; UNIV COLL LONDON HOSP, CTR ANAESTHESIA, LONDON, ENGLAND
CYA USA; SCOTLAND; ENGLAND
SO  INFECTION AND IMMUNITY, (NOV 2000) Vol. 68, No. 11, pp. 6202-6208.
    Publisher: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904.
    ISSN: 0019-9567.
DT  Article; Journal
FS  LIFE
LA  English
REC Reference Count: 40
    *ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS*
AB  Our objective is to develop a prophylactic vaccine strategy that can be
    evaluated for surgical and other high-risk hospitalized patients. In this
    paper, we describe the preparation and preclinical evaluation of a
    liposomal complete-core lipopolysaccharide (LPS) vaccine that is nontoxic
    and broadly antigenic. Complete-core (Ra-chemotype) LPSs were isolated
    from four gram-negative bacterial strains (Escherichia coli K-12, E. coli
    R1, Pseudomonas aeruginosa PAC608, and Bacteroides fragilis), mixed
    together to form a cocktail of complete-core LPSs, and then incorporated
    into multilamellar liposomes consisting of dimyristoyl phosphatidyl
    choline, dimyristoyl phosphatidylglycerol, and cholesterol in a 4:1:4
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molar ratio. The endotoxic activities of these LPS-containing liposomes were less than 0.1% of the endotoxicities of the original free LPSs as measured by the Limulus amoebocyte lysate assay. In vivo administration of liposomal complete-core LPS mixed with Al(OH)(3) to rabbits resulted in no pyrogenicity or overt toxicity over a 7-day period. In immunoblots, sera from rabbits following active immunization elicited cross-reactive antibodies to a large panel of rough and smooth LPSs from numerous clinically relevant gram-negative bacteria, including E. coli (serotypes O1, O4, O6, O8, O12, O15, O18, O75, O86, O157, and O111), P. aeruginosa (Fisher-Devlin serotypes 1, 2, and 3, which correspond to International Antigenic Typing Scheme types 6, 11, and 2, respectively), Klebsiella pneumoniae (serotypes O1, O2ab, and O3), B. fragilis, and Bacteroides valgatus, Active immunization of mice with liposomal complete-core LPS provided protection against a lethal challenge with E, coli O18 LPS, The vaccine tested was nontoxic, nonpyrogenic, and immunogenic against a wide variety of pathogens found in clinical settings.

L2 ANSWER 2 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 2000:411412 SCISEARCH
GA The Genuine Article (R) Number: 318CM
TI Excessive use of hetastarch: An iatrogenic cause of bleeding and hypocalcemia? In response
AU Gan T J (Reprint); ***BennettGuerrero E*** ; Mythen M G
CS DUKE UNIV, MED CTR, DURHAM, NC 27710 (Reprint); COLUMBIA UNIV COLL PHYS & SURG, NEW YORK, NY 10032; UNIV COLL LONDON HOSP, LONDON, ENGLAND
CYA USA; ENGLAND
SO ANESTHESIA AND ANALGESIA, (JUN 2000) Vol. 90, No. 6, pp. 1456-1456.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-2999.
DT Letter; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 9

L2 ANSWER 3 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 2000:267885 SCISEARCH
GA The Genuine Article (R) Number: 299GZ
TI Exposure to Bacteroides fragilis endotoxin during cardiac surgery
AU ***BennettGuerrero E (Reprint)*** ; Barclay G R; Youssef M E; Hossain S; VelaCantos F; Andres L A; Poxton I R
CS COLUMBIA UNIV COLL PHYS & SURG, DEPT ANESTHESIOL, 630 W 168TH ST, NEW YORK, NY 10032 (Reprint); MT SINAI SCH MED, DEPT ANESTHESIOL, NEW YORK, NY; MT SINAI SCH MED, DEPT BIOMATH, NEW YORK, NY; SCOTTISH NATL BLOOD TRANSFUS SERV, EDINBURGH, MIDLOTHIAN, SCOTLAND; UNIV EDINBURGH, SCH MED, DEPT MED MICROBIOL, EDINBURGH EH8 9AG, MIDLOTHIAN, SCOTLAND
CYA USA; SCOTLAND
SO ANESTHESIA AND ANALGESIA, (APR 2000) Vol. 90, No. 4, pp. 819-823.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-2999.
DT Article; Journal
FS LIFE; CLIN
LA English

REC Reference Count: 21

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Although endotoxemia has been observed during cardiac surgery, the identity of endotoxins to which patients are exposed is unknown. We tested the hypothesis that antibodies to Bacteroides fragilis tan anaerobic gut commensal and a common pathogen) decrease during cardiac surgery, thereby reflecting systemic exposure to this type of endotoxin. Serum antiendotoxin antibody levels were measured in 55 patients during routine cardiac surgery at the following times: Preoperatively, Pre-CPB (immediately before initiation of cardiopulmonary bypass [CPB]), Pre-CPB +5 (5 min after initiation of CPB), and End tend of surgery). Antiendotoxin antibody levels were determined by using enzyme-linked immunosorbent assay. Total immunoglobulin M (IgM) levels were measured by using laser nephelometry and decreases in total IgM levels were used to control changes in antiendotoxin antibody levels attributable to hemodilution. Median (interquartile range) hemodilution corrected IgM anti-B fragilis antibody levels decreased by 12% (5%-20%) from Preoperatively to End of surgery ($P < 0.001$). In contrast, median hemodilution corrected anti-B fragilis antibody levels did not change significantly from Pre-CPB to Pre-CPB +5, validating the correction for hemodilution. Immunoglobulin G anti-B fragilis antibody levels and IgM and immunoglobulin G anticore antibody levels decreased similarly during surgery. Intraoperatively, levels of anti-B fragilis endotoxin antibodies decreased significantly out of proportion to hemodilution. These results suggest that cardiac surgical patients are exposed to B fragilis endotoxin. implications: We prospectively measured hemodilution-corrected antiendotoxin antibody levels in 55 cardiac surgical patients. We observed significant decreases in hemodilution-corrected levels of antibody to both Bacteroides fragilis and the core of endotoxin.

L2 ANSWER 4 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)

AN 2000:331202 SCISEARCH

GA The Genuine Article (R) Number: 294NV

TI Dogs and pigs survive 2 and 1 hour near-freezing circulatory arrests after complete blood substitution with Hextend

AU Letsou G V (Reprint); ***BennettGuerrero E*** ; Sekaran P; Breznock E M; Whitehair J; Sternberg H; Jacobs R; Leavitt M L; Shermer S; Kehrer S; Voelker M; Segall J M; Waitz H D; Segall P E

CS COLUMBIA UNIV COLL PHYS & SURG, NEW YORK, NY 10032; MT SINAI MED CTR, NEW YORK, NY 10029; UNIV TEXAS, HOUSTON, TX 77030; BIOTIME INC, BERKELEY, CA 94710

CYA USA

SO FASEB JOURNAL, (15 MAR 2000) Vol. 14, No. 4, pp. A612-A612.
Publisher: FEDERATION AMER SOC EXP BIOL, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814-3998.
ISSN: 0892-6638.

DT Conference; Journal

FS LIFE

LA English

REC Reference Count: 0

L2 ANSWER 5 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)

AN 2000:830901 SCISEARCH

GA The Genuine Article (R) Number: 351BU

TI Detection of patent foramen ovale through pulse oxymetry with provocative maneuvers
AU Sukernik M R (Reprint); Kachulis B; Mets B; ***BennettGuerrero E***
CS COLUMBIA UNIV, NEW YORK, NY
CYA USA
SO ANESTHESIOLOGY, (SEP 2000) Vol. 93, No. 3A, Supp. [S], pp. A575-A575.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 6 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 2000:830842 SCISEARCH
GA The Genuine Article (R) Number: 351BU
TI Preparation and preclinial evaluation of a novel liposomal complete-core lipopolysaccharide vaccine
AU ***BennettGuerrero E (Reprint)*** ; McIntosh T J; Barclay G R; Mythen M G; Poxton I R
CS COLUMBIA UNIV, COLL P&S, NEW YORK, NY
CYA USA
SO ANESTHESIOLOGY, (SEP 2000) Vol. 93, No. 3A, Supp. [S], pp. A508-A508.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 7 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 2000:830749 SCISEARCH
GA The Genuine Article (R) Number: 351BU
TI Comparison of thromboelastographic parameters using arterial vs venous blood samples
AU Manspeizer H E (Reprint); Imai M; Frumento R J; Mets B; ***BennettGuerrero E***
CS COLUMBIA UNIV COLL PHYS & SURG, NEW YORK, NY 10032
CYA USA
SO ANESTHESIOLOGY, (SEP 2000) Vol. 93, No. 3A, Supp. [S], pp. A410-A410.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 8 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 2000:114956 SCISEARCH
GA The Genuine Article (R) Number: 279FQ
TI Preoperative antiendotoxin immune status and morbidity following

non-cardiac surgery
AU ***BennettGuerrero E (Reprint)*** ; Panah M H; Barclay R; Bodian C A; Winfree W J; Reich D L
CS COLUMBIA UNIV, NEW YORK, NY; MT SINAI SCH MED, NEW YORK, NY; SCOTTISH NATL BLOOD TRANSFUS SERV, EDINBURGH, MIDLOTHIAN, SCOTLAND
CYA USA; SCOTLAND
SO ANESTHESIA AND ANALGESIA, (FEB 2000) Vol. 90, No. 2, Supp. [S], pp. S112-S112.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 3

L2 ANSWER 9 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 2000:290687 SCISEARCH
GA The Genuine Article (R) Number: 300HE
TI Effect of hematocrit on neurological recovery in a porcine model of profound hypothermic (approximate to 3 degrees C) circulatory arrest (PHCA)
AU Sekaran P (Reprint); Ehrlich M; Hagl C; McCullough J N; Griepp R B; Wolfe D; ***BennettGuerrero E***
CS CUNY MT SINAI SCH MED, DEPT ANESTHESIOL, NEW YORK, NY 10029; CUNY MT SINAI SCH MED, DEPT CARDIAC SURG, NEW YORK, NY 10029
CYA USA
SO ANESTHESIA AND ANALGESIA, (APR 2000) Vol. 90, No. 4, Supp. [S], pp. SCA41-SCA41.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 4

L2 ANSWER 10 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 2000:57544 SCISEARCH
GA The Genuine Article (R) Number: 273XZ
TI Automated detection of gastric luminal partial pressure of carbon dioxide during cardiovascular surgery using the Tonocap
AU ***BennettGuerrero E (Reprint)*** ; Panah M H; Bodian C A; Methikalam B J; Alfarone J R; DePerio M; Mythen M G
CS COLUMBIA UNIV COLL PHYS & SURG, DEPT ANESTHESIOL, 630 W 168TH ST, NEW YORK, NY 10032 (Reprint); MT SINAI SCH MED, DEPT ANESTHESIOL, NEW YORK, NY
CYA USA
SO ANESTHESIOLOGY, (JAN 2000) Vol. 92, No. 1, pp. 38-45.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 530 WALNUT ST, PHILADELPHIA, PA 19106-3621.
ISSN: 0003-3022.
DT Article; Journal
FS LIFE; CLIN
LA English

REC Reference Count: 34

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Background: A new automated system of air tonometry (Tonocap; Datex Ohmeda, Helsinki, Finland) allows for frequent (every 15 min) measurement of gastric luminal partial pressure of carbon dioxide. Its use has not been described in cardiac surgical patients.

Methods: One hundred patients undergoing coronary artery bypass graft or cardiac valve surgery were enrolled in a prospective cohort study. After anesthetic induction and insertion of a TRIP NGS Catheter (Datex Ohmeda), measurements of gastric luminal partial pressure of carbon dioxide were obtained using the Tonocap, and gastric mucosal pH (pHi) was calculated. The main outcome measure was postoperative complication, defined as either in-hospital death or prolonged postoperative hospitalization (> 14 days).

Results: Four patients (4%) died, all of multiple-system organ failure, one each on postoperative days 9, 26, 46, and 121, Postoperative complication occurred in 18 patients (18%), all of whom exhibited persistent dysfunction of at least one organ system, Perioperatively, an abnormal pHi (< 7.32) and gastric luminal minus arterial partial pressure of carbon dioxide gap (> 8 mmHg) occurred in 66% and 70% of patients, respectively. Predictors of postoperative complication included postoperative pHi (P = 0.001), gastric luminal partial pressure of carbon dioxide (P = 0.022), and gastric luminal minus arterial partial pressure of carbon dioxide gap (P = 0.013). In contrast, arterial base excess (P > 0.4) and routinely measured hemodynamic variables (e.g., heart rate, blood pressure) were either less predictive compared with Tonocap-derived variables or not predictive,

Conclusions: Despite a low mortality rate, patients undergoing cardiac surgery exhibited high incidences of prolonged hospitalization and postoperative morbidity. The Tonocap was easy to use, particularly compared with saline tonometry, Several Tonocap-derived variables were predictive of postoperative complications consistent with previously published data using saline tonometry.

L2 ANSWER 11 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)

AN 1999:422932 SCISEARCH

GA The Genuine Article (R) Number: 200PE

TI epsilon-aminocaproic acid administration and stroke following coronary artery bypass graft surgery

AU ***BennettGuerrero E (Reprint)*** ; Spillane W F; White W D; Muhlbaier L H; Gall S A; Smith P K; Newman M F

CS MT SINAI MED CTR, DEPT ANESTHESIOL, BOX 1010, 1 GUSTAVE L LEVY PL, NEW YORK, NY 10029 (Reprint); DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710; DUKE UNIV, MED CTR, DEPT COMMUNITY & FAMILY MED, DURHAM, NC 27710; DUKE UNIV, MED CTR, DEPT NEUROL, DURHAM, NC; DUKE UNIV, MED CTR, DEPT SURG, DURHAM, NC 27710

CYA USA

SO ANNALS OF THORACIC SURGERY, (MAY 1999) Vol. 67, No. 5, pp. 1283-1287.
Publisher: ELSEVIER SCIENCE INC, 655 AVENUE OF THE AMERICAS, NEW YORK, NY 10010.
ISSN: 0003-4975.

DT Article; Journal

FS LIFE; CLIN

LA English

REC Reference Count: 20
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background. epsilon-aminocaproic acid is routinely used to reduce bleeding during cardiac surgery. Anecdotal reports of thrombotic complications have led to speculation regarding this drug's safety. We investigated the association between epsilon-aminocaproic acid administration and postoperative stroke.

Methods. Six thousand two hundred ninety-eight patients undergoing isolated coronary artery bypass graft surgery between 1989 and 1995 were studied. Data was obtained from the Duke Cardiovascular Database as well as from an automated intraoperative anesthesia record keeper. Patients identified as having postoperative stroke were reviewed and confirmed by a board certified neurologist blinded to epsilon-aminocaproic acid administration.

Results. Postoperative stroke occurred in 97 patients (1.5%). Three thousand one hundred thirty-five (49.8%) patients received epsilon-aminocaproic acid. Increased age was associated with a higher incidence of postoperative stroke ($p = 0.0001$). In contrast, there was no significant difference ($p = 0.7370$) in the incidence of stroke between use of epsilon-aminocaproic acid (1.3%) and nonuse (1.7%). Multivariable logistic regression found no significant effect of epsilon-aminocaproic acid use on stroke after accounting for age, date of surgery, and history of diabetes.

Conclusions. This series suggests that epsilon-aminocaproic acid administration does not increase the risk of postoperative stroke. (Ann Thorac Surg 1999;67:1283-7) (C) 1999 by The Society of Thoracic Surgeons.

L2 ANSWER 12 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1999:357016 SCISEARCH
GA The Genuine Article (R) Number: 192DM
TI Hextend(R), a physiologically balanced plasma expander for large volume use in major surgery: A randomized phase III clinical trial
AU Gan T J (Reprint); ***BennettGuerrero E*** ; PhillipsBute B; Wakeling H; Moskowitz D M; Olufolabi Y; Konstadt S N; Bradford C; Glass P S A; Machin S J; Mythen M G
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, BOX 3094, DURHAM, NC 27710 (Reprint); MT SINAI MED CTR, DEPT ANESTHESIOL, NEW YORK, NY 10029; UNIV COLL LONDON HOSP, DEPT HAEMATOL, LONDON, ENGLAND; UNIV COLL LONDON HOSP, DEPT ANAESTHESIA, LONDON, ENGLAND
CYA USA; ENGLAND
SO ANESTHESIA AND ANALGESIA, (MAY 1999) Vol. 88, No. 5, pp. 992-998.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-2999.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 19
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Hestend((R)) (BioTime, Inc., Berkeley, CA) is a new plasma volume expander containing 6% hetastarch, balanced electrolytes, a lactate buffer, and physiological levels of glucose. In preclinical studies, its use in shock models was associated with an improvement in outcome compared with alternatives, such as albumin or 6% hetastarch in saline. In a

prospective, randomized, two-center study (n = 120), we compared the efficacy and safety of Hextend((R)) versus 6% hetastarch in saline (HES) for the treatment of hypovolemia during major surgery. Patients at one center had a blood sample drawn at the beginning and the end of surgery for thromboelastographic (TEG) analysis. Hextend((R)) was as effective as HES for the treatment of hypovolemia. Patients received an average of 1596 mt of Hestend((R)): 42% received >20 mL/kg up to a total of 5000 mt. No patient received albumin. Hextend((R))-treated patients required less intraoperative calcium (4 vs 220 mg; P < 0.05). In a subset analysis of patients receiving red blood cell transfusions (n = 56; 47%), Hextend((R))-treated patients had a lower mean estimated blood loss (956 mt less; P = 0.02) and were less likely to receive calcium supplementation (P = 0.04). Patients receiving HES demonstrated significant prolongation of time to onset of clot formation (based on TEG) not seen in the Hextend((R)) patients (P < 0.05). No Hextend((R)) patient experienced a related serious adverse event, and there was no difference in the total number of adverse events between the two groups. The results of this study demonstrate that Hextend((R)), with its novel buffered, balanced electrolyte formulation, is as effective as 6% hetastarch in saline for the treatment of hypovolemia and may be a safe alternative even when used in volumes up to 5 L. Implications: Hextend((R)) (BioTime, Inc., Berkeley, CA) is a new plasma volume expander containing 6% hetastarch, balanced electrolytes, a lactate buffer, and a physiological level of glucose. It is as effective as 6% hetastarch in saline for the treatment of hypovolemia but has a more favorable side effects profile in volumes of up to 5 L compared with 6% hetastarch in saline.

L2 ANSWER 13 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1999:539951 SCISEARCH
GA The Genuine Article (R) Number: 211KG
TI Variation of endogenous endotoxin immunity between UK and US surgical patients
AU Grocott M (Reprint); HamiltonDavies C; Barclay G R; Calvano S; Lowry S; ***BennettGuerrero E*** ; Mythen M G
CS UCLH, LONDON, ENGLAND; SNBTS, EDINBURGH, MIDLOTHIAN, SCOTLAND; UNIV MED & DENT NEW JERSEY, ROBERT WOOD JOHNSON MED SCH, NEW BRUNSWICK, NJ; MT SINAI MED CTR, NEW YORK, NY 10029
CYA ENGLAND; SCOTLAND; USA
SO BRITISH JOURNAL OF ANAESTHESIA, (JUN 1999) Vol. 82, Supp. [1], pp. A568-A568.
Publisher: PROF SCI PUBL, TAVISTOCK HOUSE EAST, TAVISTOCK SQUARE, LONDON WC1H 9JR, ENGLAND.
ISSN: 0007-0912.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 2

L2 ANSWER 14 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1999:609686 SCISEARCH
GA The Genuine Article (R) Number: 222DD
TI The use of a postoperative morbidity survey to evaluate patients with prolonged hospitalization after routine, moderate-risk, elective surgery
AU ***BennettGuerrero E (Reprint)*** ; Welsby I; Dunn T J; Young L R; Wahl

T A; Diers T L; PhillipsBute B G; Newman M F; Mythen M G
CS COLUMBIA UNIV COLL PHYS & SURG, DEPT ANESTHESIOL, 630 W 168TH ST, P&S BOX 46, NEW YORK, NY 10032 (Reprint); MT SINAI MED CTR, DEPT ANESTHESIOL, NEW YORK, NY 10029; DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC; DUKE UNIV, MED CTR, DEPT BIOSTAT, DURHAM, NC; UNIV COLL LONDON HOSP, DEPT ANAESTHESIA, LONDON, ENGLAND
CYA USA; ENGLAND
SO ANESTHESIA AND ANALGESIA, (AUG 1999) Vol. 89, No. 2, pp. 514-519.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-2999.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 32
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Vital healthcare resources are devoted to caring for patients with prolonged hospitalization after routine, moderate-risk surgery. Despite the significant cost,little is known about the overall incidence and pattern of complications in these patients. Four hundred thirty-eight patients undergoing a diverse group of routine, moderate-risk, elective surgical procedures were enrolled into a prospective, blinded, cohort study. Complications were assessed using a postoperative morbidity survey. The main outcome was postoperative complication, defined as either in-hospital death or prolonged postoperative hospitalization (>7 days). The mortality rate was 1.6%. Postoperative complications occurred in 118 patients (27% [95% CI 23-31]). Complications frequently observed in these patients included: gastrointestinal 51% (42-60), pulmonary 25% (17-33), renal 21% (14-28), and infectious 13% (7-19). Most complications were not directly related to the type/site of surgery. indices of tissue trauma (blood loss [P < 0.001], surgical duration [P = 0.001]) and tissue perfusion (arterial base deficit [P = 0.008], gastric pHi [P = 0.02]) were the strongest intraoperative predictors of complications. Despite a low mortality rate, we found that complications after routine, moderate-risk, elective surgery are common and involve multiple organ systems. Our 9-point survey can be used by healthcare providers and payers to characterize postoperative morbidity in their respective settings. Implications: Little is known about the overall incidence and pattern of complications in patients with prolonged hospitalization after routine, elective surgery. We prospectively assessed these complications using a novel postoperative morbidity survey. The postoperative morbidity survey can be used in future clinical outcome trials, as well as in routine hospital-based quality assurance.

L2 ANSWER 15 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1999:139083 SCISEARCH
GA The Genuine Article (R) Number: 165EN
TI How do anesthesiologists define abnormal heart rate and blood pressure?
AU Reich D L (Reprint); Pavone L; ***BennettGuerrero E*** ; Krol M
CS MT SINAI SCH MED, DEPT ANESTHESIOL, NEW YORK, NY
CYA USA
SO ANESTHESIA AND ANALGESIA, (FEB 1999) Vol. 88, No. 2, Supp. [S], pp. S192-S192.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ,

PHILADELPHIA, PA 19106.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 16 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1999:866950 SCISEARCH
GA The Genuine Article (R) Number: 234JH
TI Comparison of intraoperative blood loss in patients undergoing major surgery using Hextend, Hespan and lactated Ringer's solution.
AU Martin G (Reprint); ElMoalem H; ***BennettGuerrero E*** ; Mythen M G; Gan T J
CS DUKE UNIV, MED CTR, DURHAM, NC
CYA USA
SO ANESTHESIOLOGY, (SEP 1999) Vol. 91, No. 3A, Supp. [S], pp. A166-A166.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 17 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1999:138990 SCISEARCH
GA The Genuine Article (R) Number: 165EN
TI Do hemodynamic abnormalities influence mortality and length of stay in noncardiac surgery?
AU Reich D L (Reprint); Pavone L; ***BennettGuerrero E*** ; Krol M
CS MT SINAI SCH MED, DEPT ANESTHESIOL, NEW YORK, NY
CYA USA
SO ANESTHESIA AND ANALGESIA, (FEB 1999) Vol. 88, No. 2, Supp. [S], pp. S98-S98.
Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 18 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1999:360079 SCISEARCH
GA The Genuine Article (R) Number: 185GH
TI Anti-endotoxin neutralizing activity of serum in patients prior to cardiac surgery: Relationship to EndoCAb levels
AU ***BennettGuerrero E (Reprint)*** ; Barclay G R; Weng P; Andres L A; VelaCantos F; Bodian C A
CS MT SINAI MED CTR, DEPT ANESTHESIOL, NEW YORK, NY 10029
CYA USA
SO ANESTHESIA AND ANALGESIA, (APR 1999) Vol. 88, No. 4, Supp. [S], pp. U46-U46.

Publisher: LIPPINCOTT WILLIAMS & WILKINS, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 3

L2 ANSWER 19 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:768239 SCISEARCH
GA The Genuine Article (R) Number: 117YR
TI Automated detection of gastric mucosal hypoperfusion during cardiovascular surgery using the Tonocap(TM)
AU ***BennettGuerrero E (Reprint)*** ; Devine P; Panah M H; Methikalam B J; Alfarone J R; DePerio M; Mythen M G
CS CUNY, MT SINAI MED CTR, DEPT ANESTHESIOL, NEW YORK, NY 10029
CYA USA
SO ANESTHESIOLOGY, (SEP 1998) Vol. 89, No. 3A, Supp. [S], pp. A968-A968.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 20 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:188075 SCISEARCH
GA The Genuine Article (R) Number: YZ516
TI Could we know epsilon-aminocaproic acid level during cardiopulmonary bypass? Response
AU ***BennettGuerrero E (Reprint)*** ; Mythen M G
CS MT SINAI MED CTR, DEPT ANESTHESIOL, NEW YORK, NY 10029 (Reprint)
CYA USA
SO ANESTHESIA AND ANALGESIA, (MAR 1998) Vol. 86, No. 3, pp. 680-681.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Letter; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 2

L2 ANSWER 21 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:721783 SCISEARCH
GA The Genuine Article (R) Number: 118FU
TI Acute depression of myocardial beta-adrenergic receptor signaling during cardiopulmonary bypass - Impairment of the adenylyl cyclase moiety
AU Booth J V; Landolfo K P; Chesnut L C; ***BennettGuerrero E*** ; Gerhardt M A; Atwell D N; ElMoalem H E; Smith M S; Funk B L; Kuhn C M; Kwatra M M; Schwinn D A (Reprint)
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, BOX 3094, DURHAM, NC 27710 (Reprint); DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710
CYA USA

SO ANESTHESIOLOGY, (SEP 1998) Vol. 89, No. 3, pp. 602-611.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-3022.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 47
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background: Previously the authors showed that myocardial beta-adrenergic (beta AR) function is reduced after cardiopulmonary bypass (CPB) in a canine model. Whether CPB results in similar effects on beta AR function in adult humans is not known. Therefore the current study tested two hypotheses: (1) That myocardial beta AR signaling is reduced in adult humans after CPB, and (2) that administration of long-term preoperative beta AR antagonists prevents this process.

Methods: After they Save informed consent, 52 patients undergoing aortocoronary surgery were enrolled. Atrial biopsies were obtained before CPB and immediately before discontinuation of CPB. Plasma catecholamine concentrations, myocardial beta AR density, and functional responsiveness (basal, isoproterenol, zinterol, sodium fluoride, and manganese-stimulated adenylyl cyclase activity) were assessed.

Results: Catecholamine levels increased significantly during CPB ($P < 0.005$). Myocardial beta AR adenylyl cyclase coupling decreased during CPB, as evidenced by a 21% decrease in isoproterenol-stimulated adenylyl cyclase activity (750 [430] pmol cyclic adenosine monophosphate per milligram total protein 15 min before CPB compared with 540 [390] at the end of CPB, $P = 0.0062$, medians [Interquartile range]) despite constant beta AR density. Differential activation along the beta AR signal transduction cascade localized the defect to the adenylyl cyclase moiety Administration of long-term preoperative beta AR antagonists did not prevent acute CPB-induced myocardial beta AR dysfunction.

Conclusions: These data indicate that the myocardial adenylyl cyclase response to beta AR agonists decreases acutely in adults during aortocoronary surgery requiring CPB, regardless of whether long-term preoperative beta AR antagonists are administered. The mechanism underlying acute beta AR dysfunction appears to be direct impairment of the adenylyl cyclase moiety. Similar increases in manganese-stimulated activity before and at the end of CPB show preserved adenylyl cyclase catalytic activity, suggesting that other mechanisms (such as decreased protein levels or altered isoform expression or function) may be responsible for decreased adenylyl cyclase function.

L2 ANSWER 22 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:109458 SCISEARCH
GA The Genuine Article (R) Number: YU349
TI Treatment of myxedema coma for emergency surgery - Reply
AU ***BennettGuerrero E (Reprint)*** ; Schwinn D A
CS MT SINAI MED CTR, DEPT ANESTHESIOL, NEW YORK, NY 10029 (Reprint); DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710
CYA USA
SO ANESTHESIA AND ANALGESIA, (FEB 1998) Vol. 86, No. 2, pp. 451-451.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.

ISSN: 0003-2999.
DT Letter; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 23 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:767582 SCISEARCH
GA The Genuine Article (R) Number: 117YR
TI Comparison of intraoperative administration of Hextend(R) vs. Hespan(R) for the treatment of hypovolemia during major surgery
AU Gan T J (Reprint); ***BennettGuerrero E*** ; Glass P S A; Moskowitz D M; Robertson K; PhillipsBute B; Konstadt S; Hilton A B; Kuemeroski D; Dufore S; Mythen M G
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710; MT SINAI MED CTR, NEW YORK, NY 10029
CYA USA
SO ANESTHESIOLOGY, (SEP 1998) Vol. 89, No. 3A, Supp. [S], pp. A305-A305.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 2

L2 ANSWER 24 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:296467 SCISEARCH
GA The Genuine Article (R) Number: ZF995
TI Heparin-associated antibodies and adverse outcomes following cardiac surgery
AU Watke C M (Reprint); ***BennettGuerrero E*** ; White W D; Slaughter T F
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710; DURHAM VET AFFAIRS MED CTR, DURHAM, NC 27710
CYA USA
SO ANESTHESIA AND ANALGESIA, (APR 1998) Vol. 86, No. 4, Supp. [S], pp. SC116-SC116.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 2

L2 ANSWER 25 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 1998:296401 SCISEARCH
GA The Genuine Article (R) Number: ZF995
TI Morbidity associated with prolonged hospital length of stay following cardiac surgery
AU Panah M (Reprint); Andres L A; Strope S A; VelaCantos F; ***BennettGuerrero E***
CS CUNY, MT SINAI MED CTR, DEPT ANESTHESIOL, NEW YORK, NY 10029
CYA USA

SO ANESTHESIA AND ANALGESIA, (APR 1998) Vol. 86, No. 4, Supp. [S], pp. SCA50-SCA50.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 0

L2 ANSWER 26 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 97:919661 SCISEARCH
GA The Genuine Article (R) Number: YK509
TI Cost-benefit and efficacy of aprotinin compared with epsilon-aminocaproic acid in patients having repeated cardiac operations - A randomized, blinded clinical trial
AU ***BennettGuerrero E (Reprint)*** ; Sorohan J G; Gurevich M L; Kazanjian P E; Levy R R; Barbera A V; White W D; Slaughter T F; Sladen R N; Smith P K; Newman M F
CS MT SINAI MED CTR, DEPT ANESTHESIOL, BOX 1010, 1 GUSTAVE L LEVY PL, NEW YORK, NY 10029 (Reprint); DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710; FDN FAVALORO, DEPT ANESTHESIOL, BUENOS AIRES, DF, ARGENTINA; DUKE UNIV, MED CTR, DEPT SURG, DURHAM, NC 27710
CYA USA; ARGENTINA
SO ANESTHESIOLOGY, (DEC 1997) Vol. 87, No. 6, pp. 1373-1380.
Publisher: LIPPINCOTT-RAVEN PUBL, 227 EAST WASHINGTON SQ, PHILADELPHIA, PA 19106.
ISSN: 0003-3022.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 40
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Background: Aprotinin and epsilon-aminocaproic acid are routinely used to reduce bleeding during cardiac surgery, The marked difference in average wholesale cost between these two drug therapies (aprotinin, $1,080 vs. epsilon-aminocaproic acid, $11) has generated significant controversy regarding their relative efficacies and costs,

Methods: in a multicenter, randomized, prospective, blinded trial patients having repeated cardiac surgery received either a high-dose regimen of aprotinin (total dose, 6 x 10(6) kallikrein inactivator units) or epsilon-aminocaproic acid (total dose, 270 mg/kg).

Results: Two hundred four patients were studied Overall (data are median [25th-75th percentiles]), aprotinin-treated patients had less postoperative thoracic drainage (511 ml[383-805 mi] vs. 655 mi [464-1,045 ml]: P -0.016) and received fewer platelet transfusions (0 [range, 0-1] vs. [range, 0-2]; P = 0.036). The surgical field was more likely to be considered free of bleeding in aprotinin-treated patients (44% vs. 26%; P = 0.012), No differences, however, were seen in allogeneic erythrocyte transfusions or in the time required for chest closure, Overall, direct and indirect bleeding-related costs were greater in aprotinin-than in epsilon-aminocaproic acid-treated patients ($1,813 [$1,476-2,605] vs. $1,088 [range, $511-2,057]; P = 0.0001). This difference in cost per case varied in magnitude among sites but not in direction.

Conclusions: Aprotinin was more effective than epsilon-aminocaproic acid at decreasing bleeding and platelet transfusions. epsilon-aminocaproic acid however, was the more cost-effective therapy over a broad range of estimates for bleeding-related costs in patients undergoing repeated cardiac surgery, A cost-benefit analysis using the lower cost of half-dose aprotinin ($540) still resulted in a significant cost advantage using epsilon-aminocaproic therapy (P = 0.022).

L2 ANSWER 27 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 97:161128 SCISEARCH
GA The Genuine Article (R) Number: WJ498
TI Relationship of preoperative antiendotoxin core antibodies and adverse outcomes following cardiac surgery
AU ***BennettGuerrero E (Reprint)*** ; Ayuso L; HamiltonDavies C; White W D; Barclay G R; Smith P K; King S A; Muhlbaier L H; Newman M F; Mythen M G
CS MT SINAI MED CTR, DEPT ANESTHESIOL, BOX 1010, 1 GUSTAVE L LEVY PL, NEW YORK, NY 10029 (Reprint); HARVARD UNIV, SCH MED, BOSTON, MA; MIDDLESEX HOSP, DEPT ANESTHESIOL, LONDON, ENGLAND; DUKE UNIV, MED CTR, DUKE HEART CTR, DEPT ANESTHESIOL, DURHAM, NC 27710; DUKE UNIV, MED CTR, DUKE HEART CTR, DEPT SURG, DURHAM, NC 27710; DUKE UNIV, MED CTR, DUKE HEART CTR, DEPT COMMUNITY & FAMILY MED, DURHAM, NC 27710; SCOTTISH NATL BLOOD TRANSFUS SERV, EDINBURGH, MIDLOTHIAN, SCOTLAND
CYA USA; ENGLAND; SCOTLAND
SO JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, (26 FEB 1997) Vol. 277, No. 8, pp. 646-650.
Publisher: AMER MEDICAL ASSOC, 515 N STATE ST, CHICAGO, IL 60610.
ISSN: 0098-7484.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 51
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Objective.-To test the hypothesis that low serum antiendotoxin core antibody (EndoCAb) level is an independent predictor of adverse outcome following cardiac surgery,
Design.-Prospective, blinded, cohort study.
Setting.-Tertiary care medical center.
Subjects.-A total of 301 patients undergoing coronary artery bypass graft surgery and/or valvular heart surgery.
Design.-Preoperative serum was assayed for IgM EndoCAb, IgG EndoCAb, total IgM, and total IgG levels. Known preoperative risk factors were assessed, and patients were assigned a risk score using a validated method,
Main Outcome Measure.-A major complication, defined as either in-hospital death or postoperative length of stay greater than 10 days,
Results.-Overall, a major complication occurred in 34 patients (11.3%), Lower IgM EndoCAb level independently predicted (P=.002) increased risk of major complication over and above the effects of preoperative risk score (P=.02), total IgG level (P=.07), and all other known perioperative risk factors. In contrast, IgG EndoCAb and total IgM concentrations did not predict outcome, No association existed between risk score and level of IgM EndoCAb.
Conclusion.-There is marked preoperative variability in humoral immunity against endotoxin core, which is not accounted for by differences

in known preoperative risk factors. In this study, low levels of IgMEndoCAb were an important independent predictor of adverse postoperative outcome, which supports the theory that endotoxemia is a cause of postoperative morbidity.

L2 ANSWER 28 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 97:593878 SCISEARCH
GA The Genuine Article (R) Number: XP077
TI epsilon-aminocaproic acid plasma levels during cardiopulmonary bypass
AU ***BennettGuerrero E (Reprint)*** ; Sorohan J G; Canada A T; Ayuso L; Newman M F; Reves J G; Mythen M G
CS MT SINAI MED CTR, DEPT ANESTHESIOL, BOX 1010, 1 GUSTAVE L LEVY PL, NEW YORK, NY 10029 (Reprint); DUKE UNIV, MED CTR, DUKE HEART CTR, DURHAM, NC 27710; HARVARD UNIV, SCH MED, BOSTON, MA; MIDDLESEX HOSP, LONDON, ENGLAND
CYA USA; ENGLAND
SO ANESTHESIA AND ANALGESIA, (AUG 1997) Vol. 85, No. 2, pp. 248-251.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 14
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB epsilon-Aminocaproic acid (EACA) concentrations achieved during cardiopulmonary bypass (CPB) have not been previously reported. It is unknown whether plasma concentrations reported to inhibit fibrinolysis in vitro (130 mu g/mL) are achieved or whether differences in these levels relate to variability in postoperative bleeding. EACA (total intraoperative dose 270 mg/kg) was administered to 27 patients undergoing cardiac reoperation. The plasma EACA concentration was measured by using high-pressure liquid chromatography: 1) 30 min after initiation of drug administration (baseline); 2) 30 min (CPB + 30) after initiation of CPB; 3) 90 min after initiation of CPB. (CPB + 90); and 4) at cardiopulmonary bypass termination (end CPB), Plasma EACA concentrations (mu g/mL, min - max, mean +/- SD) were 276-998, 593 +/- 153 at baseline; 147-527, 302 +/- 95 at CPB + 30; 112-500, 314 +/- 100 at CPB +/- 90; and 84-537, 317 +/- 100 at end CPB. Twenty-four- hour postoperative thoracic drainage and allogeneic red blood cell transfusions were not associated with plasma levels at any time. Although plasma EACA concentrations greater than 130 mu g/mL were consistently achieved, we observed a marked variabiliy (moro than sixfold) in plasma concentrations and bleeding outcomes despite the use of a weight-based dosing regimen, This variability in drug levels appears to have little relevance to bleeding outcomes, possibly since mean plasma levels exceeded 130 mu g/mL during CPB, and nearly all patients (26 of 27) achieved that target level.

L2 ANSWER 29 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 97:128052 SCISEARCH
GA The Genuine Article (R) Number: WF780
TI Epsilon-aminocaproic acid (amicar) plasma levels during cardiopulmonary bypass
AU ***BennettGuerrero E (Reprint)*** ; Sorohan J G; Canada A T; Ayuso L; Newman M F; Reves J G; Mythen M G

CS DUKE UNIV, DEPT ANESTHESIOL, DURHAM, NC 27710
CYA USA
SO ANESTHESIA AND ANALGESIA, (FEB 1997) Vol. 84, Supp. [2], pp. S62-S62.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 4

L2 ANSWER 30 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 97:128023 SCISEARCH
GA The Genuine Article (R) Number: WF780
TI Morbidity associated with prolonged hospital length of stay following moderate and high risk elective surgery
AU ***BennettGuerrero E (Reprint)*** ; Young L R; Wahl T A; Diers T L; Mythen M G
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710
CYA USA
SO ANESTHESIA AND ANALGESIA, (FEB 1997) Vol. 84, Supp. [2], pp. S33-S33.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 3

L2 ANSWER 31 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 97:514875 SCISEARCH
GA The Genuine Article (R) Number: XH730
TI Effect of chronic and acute thyroid hormone reduction on perioperative outcome
AU ***BennettGuerrero E (Reprint)*** ; Kramer D C; Schwinn D A
CS MT SINAI MED CTR, DEPT ANESTHESIOL, BOX 1010, 1 GUSTAVE L LEVY PL, NEW YORK, NY 10029 (Reprint); DUKE UNIV, MED CTR, DUKE HEART CTR, DEPT PHARMACOL, DURHAM, NC 27710; DUKE UNIV, MED CTR, DUKE HEART CTR, DEPT SURG, DURHAM, NC 27710; DUKE UNIV, MED CTR, DUKE HEART CTR, DEPT ANESTHESIOL, DURHAM, NC 27710
CYA USA
SO ANESTHESIA AND ANALGESIA, (JUL 1997) Vol. 85, No. 1, pp. 30-36.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 68

L2 ANSWER 32 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 96:898870 SCISEARCH
GA The Genuine Article (R) Number: VV543
TI Maintenance of therapeutic: Plasma aprotinin levels during prolonged

cardiopulmonary bypass using a large-dose regimen
AU ***BennettGuerrero E (Reprint)*** ; Sorohan J G; Howell S T; Ayuso L; Cardigan R A; Newman M F; Mackie I J; Reves J G; Mythen M G
CS MT SINAI MED CTR, DEPT ANESTHESIOL, BOX 1010, 1 GUSTAVE L LEVY PL, NEW YORK, NY 10029 (Reprint); DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC 27710; HARVARD UNIV, SCH MED, BOSTON, MA; UNIV COLL LONDON, SCH MED, DEPT HAEMATOL, LONDON W1N 8AA, ENGLAND
CYA USA; ENGLAND
SO ANESTHESIA AND ANALGESIA, (DEC 1996) Vol. 83, No. 6, pp. 1189-1192.
Publisher: WILLIAMS & WILKINS, 351 WEST CAMDEN ST, BALTIMORE, MD 21201-2436.
ISSN: 0003-2999.
DT Article; Journal
FS LIFE; CLIN
LA English
REC Reference Count: 13
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Aprotinin concentrations in the range of 127-191 kallikrein inactivator units (KIU)/mL at the end of cardiopulmonary bypass (CPB) (<2 h duration) reduce transfusion requirements. It has been suggested that prolonged CPB may require higher infusion rates which significantly increase cost. We tested the hypothesis that large-dose aprotinin maintains therapeutic plasma levels during prolonged periods of CPB (>2 h). Aprotinin was administered as follows: 2 x 10(6) KIU upon skin incision; 0.5 x 10(6) KIU/h x 4-h infusion on initiation of CPB; and 2 X 10(6) KIU added to the CPB prime solution. Aprotinin activity was measured 1) 30 min after initiation of drug administration (Pre-CPB); 2) 30 min after initiation of CPB (CPB + 30); 3) 90 min after initiation of CPB (CPB + 90); and 4) at CPB termination (End CPB). CPB duration (mean +/- SD) was 158 +/- 51 min. Plasma aprotinin concentrations (KIU/mL, mean +/- SD) were: 234 +/- 30 at Pre-CPB; 229 +/- 35 at CPB + 30; 184 +/- 27 at CPB + 90; and 179 +/- 22 at End CPB. In all patients, aprotinin levels at the completion of CPB were in the range previously reported to be effective. The authors conclude that large-dose regimen limited to 6 X 10(6) KIU maintained therapeutic plasma aprotinin concentrations during prolonged CPB.

L2 ANSWER 33 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 96:161844 SCISEARCH
GA The Genuine Article (R) Number: TX174
TI CARDIOVASCULAR EFFECTS OF INTRAVENOUS TRIIODOTHYRONINE IN PATIENTS UNDERGOING CORONARY-ARTERY BYPASS GRAFT-SURGERY - A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL
AU ***BENNETTGUERRERO E (Reprint)*** ; JIMENEZ J L; WHITE W D; DAMICO E B; BALDWIN B I; SCHWINN D A
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DUKE HEART CTR, BOX 3094, DURHAM, NC, 27710 (Reprint); DUKE UNIV, MED CTR, DEPT SURG, DUKE HEART CTR, DURHAM, NC, 27710; DUKE UNIV, MED CTR, DEPT PHARMACOL, DUKE HEART CTR, DURHAM, NC, 27710
CYA USA
SO JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, (06 MAR 1996) Vol. 275, No. 9, pp. 687-692.
ISSN: 0098-7484.
DT Article; Journal
FS LIFE; CLIN

LA ENGLISH
REC Reference Count: 55
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Objective.-To test the hypothesis that triiodothyronine (T-3) administration improves hemodynamic variables and decreases inotropic drug requirements in cardiac surgery patients.

Design.-Prospective, randomized, double-blind, placebo-controlled trial.

Setting.-Tertiary care medical center.

Patients.-A total of 211 patients undergoing coronary artery surgery at high risk for requiring inotropic drug support.

Intervention.-At release of aortic cross-clamp, patients were randomized to an intravenous infusion of T-3 (0.8 mu g/kg followed by 0.12 mu g . kg(-1). h(-1) for 6 hours), dopamine (positive control, 5 mu g . kg(-1). min(-1) for 6 hours), or placebo.

Main Outcome Measures.-Perioperative hemodynamic variables, inotropic support requirements, and serum T-3 concentrations.

Results.-Mean+/-SEM free T-3 serum concentrations decreased significantly during cardiopulmonary bypass in all groups (from 0.0035+/-0.0001 nmol/L [0.23+/-0.01 ng/dl] to 0.001+/-0.0001 nmol/L. [0.07+/-0.00 ng/dl]; P=.001) and increased to 0.0133+/-0.0004 nmol/L [0.87+/-0.03 ng/dL] (twice normal range; P<.001) following initiation of intravenous T-3. Intravenous T-3 did not change hemodynamic variables or inotropic drug requirements; however, heart rate increased (P<.001), and a trend toward decreased use of inotropic agents was demonstrated in the dopamine group.

Conclusions.-Triiodothyronine administration prevents decreases in serum thyroid hormone concentrations associated with cardiopulmonary bypass. Intravenous T-3 does not have dramatic effects on hemodynamic variables in this setting as has been previously suggested. Although mild effects on myocardial performance may exist, we cannot recommend at this time the routine use of intravenous T-3 as an inotropic agent in patients undergoing coronary artery bypass graft surgery.

L2 ANSWER 34 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 96:810301 SCISEARCH
GA The Genuine Article (R) Number: VM466
TI PREOPERATIVE ANTI-ENDOTOXIN-CORE ANTIBODY LEVEL AND OUTCOME FOLLOWING CARDIAC-SURGERY
AU ***BENNETTGUERRERO E (Reprint)*** ; AYUSO L; HAMILTONDAVIES C; WHITE W D; SMITH P K; MUHLBAIER L H; NEWMAN M F; BARCLAY G R; MYTHEN M G
CS DUKE UNIV, MED CTR, DURHAM, NC, 27710; HARVARD UNIV, SCH MED, BOSTON, MA, 00000; MIDDLESEX HOSP, LONDON, ENGLAND; EDINBURGH BLOOD TRANSFUS CTR, EDINBURGH, MIDLOTHIAN, SCOTLAND
CYA USA; ENGLAND; SCOTLAND
SO ANESTHESIOLOGY, (SEP 1996) Vol. 85, No. 3A, Supp. S, pp. A254. ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 3

L2 ANSWER 35 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 96:810195 SCISEARCH

GA The Genuine Article (R) Number: VM466
TI THE HEPARIN MANAGEMENT TEST (HMT) - AN IMPROVED METHOD FOR MONITORING ANTICOAGULATION DURING CARDIAC-SURGERY
AU SLAUGHTER T F (Reprint); GROCOTT H; GREENBLO K; ***BENNETTGUERRERO E*** ; HILTON A; HODGINS L; MARK J B
CS DUKE UNIV, DEPT ANESTHESIOL, DURHAM, NC, 27710; VET AFFAIRS MED CTR, DURHAM, NC, 27710
CYA USA
SO ANESTHESIOLOGY, (SEP 1996) Vol. 85, No. 3A, Supp. S, pp. A148.
ISSN: 0003-3022.
DT Conference; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 2

L2 ANSWER 36 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 96:273913 SCISEARCH
GA The Genuine Article (R) Number: UD164
TI THE EFFECT OF TRIIODOTHYRONINE (T3) REPLACEMENT ON FREE AND TOTAL T3 LEVELS IN VALVULAR HEART-SURGERY
AU JIMENEZ J L (Reprint); ***BENNETTGUERRERO E*** ; DAMICO E B; CLEMENTS F M; VANTRIGT P; SCHWINN D A
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC, 27710; DUKE UNIV, MED CTR, DEPT PHARMACOL, DURHAM, NC, 27710; DUKE UNIV, MED CTR, DEPT SURG, DURHAM, NC, 27710
CYA USA
SO ANESTHESIA AND ANALGESIA, (APR 1996) Vol. 82, No. 4, Supp. S, pp. SC111.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 3

L2 ANSWER 37 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 96:502789 SCISEARCH
GA The Genuine Article (R) Number: UV485
TI TRIIODOTHYRONINE AND CARDIAC-SURGERY - REPLY
AU ***BENNETTGUERRERO E (Reprint)*** ; SCHWINN D A
CS DUKE UNIV, MED CTR, DURHAM, NC, 27710 (Reprint)
CYA USA
SO JAMA-JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION, (10 JUL 1996) Vol. 276, No. 2, pp. 100-101.
ISSN: 0098-7484.
DT Letter; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 3

L2 ANSWER 38 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 96:273812 SCISEARCH
GA The Genuine Article (R) Number: UD164
TI EFFECT OF LONG-CARDIOPULMONARY BYPASS DURATION ON SERUM APROTININ PHARMACOKINETICS USING A HIGH-DOSE REGIMEN
AU ***BENNETTGUERRERO E (Reprint)*** ; SOROHAN J G; AYUSO L; CARDIGAN R A;

NEWMAN M F; MACKIE I J; MYTHEN M G
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC, 27710; HARVARD UNIV, SCH MED, BOSTON, MA, 00000; UNIV COLL LONDON, LONDON, ENGLAND
CYA USA; ENGLAND
SO ANESTHESIA AND ANALGESIA, (APR 1996) Vol. 82, No. 4, Supp. S, pp. SCA10.
ISSN: 0003-2999.
DT Conference; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 4

L2 ANSWER 39 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 94:482708 SCISEARCH
GA The Genuine Article (R) Number: NZ337
TI BRONCHOSPASM AFTER INTRAVENOUS ADENOSINE ADMINISTRATION
AU ***BENNETTGUERRERO E*** ; YOUNG C C (Reprint)
CS DUKE UNIV, MED CTR, DEPT ANESTHESIOL, BOX 3094, DURHAM, NC, 27710 (Reprint); DUKE UNIV, MED CTR, DEPT ANESTHESIOL, DURHAM, NC, 27710
CYA USA
SO ANESTHESIA AND ANALGESIA, (AUG 1994) Vol. 79, No. 2, pp. 386-388.
ISSN: 0003-2999.
DT Note; Journal
FS LIFE; CLIN
LA ENGLISH
REC Reference Count: 21

L2 ANSWER 40 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 93:220988 SCISEARCH
GA The Genuine Article (R) Number: KV271
TI RESPONSE OF THE HYPERTROPHIED LEFT-VENTRICLE TO TACHYCARDIA - IMPORTANCE OF MATURATION
AU FUJII A M (Reprint); AOYAGI T; FLANAGAN M F; TAKAHASHI T; ***BENNETTGUERRERO E*** ; COLAN S D; IZUMO S
CS CHILDRENS HOSP MED CTR, JOINT PROGRAM NEONATOL, 300 LONGWOOD AVE, BOSTON, MA, 02115 (Reprint); HARVARD UNIV, SCH MED, DEPT PEDIAT, BOSTON, MA, 02115; HARVARD UNIV, SCH MED, DEPT MED, BOSTON, MA, 02115; BETH ISRAEL HOSP, MOLEC MED UNIT, BOSTON, MA, 02215; BETH ISRAEL HOSP, DIV CARDIOVASC, BOSTON, MA, 02215; CHILDRENS HOSP MED CTR, DEPT CARDIOL, BOSTON, MA, 02115
CYA USA
SO AMERICAN JOURNAL OF PHYSIOLOGY, (MAR 1993) Vol. 264, No. 3, Part 2, pp. H983-H993.
ISSN: 0002-9513.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 36
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS
AB Pressure overload left ventricular (LV) hypertrophy (LVH) induces ventricular dysfunction during stress, which is commonly attributed to diminished myocardial capillary density and ischemia. Immature hearts with LVH have a normal coronary flow reserve and capillary density. The purpose of this study was to determine 1) whether young lambs with LVH had an abnormal response to chronotropic stress, 2) whether nonischemic mechanisms contributed to the abnormal response, and 3) whether the age at

which LVH was induced affected the response. We assessed LV endomyocardial function, perfusion, and Ca2+-adenosinetriphosphatase (ATPase) mRNA levels in chronically instrumented lambs with and without LVH and adult sheep with and without LVH. Rapid pacing induced diastolic dysfunction, increased time constant of isovolumic relaxation using an iterative fit (t(M)), and elevated LV diastolic pressures in young lambs and adult sheep with LVH. During pacing, t(M) was greater in the adult sheep with LVH than in the young lambs with LVH. Ca2+-ATPase mRNA levels were 79% less in adult sheep with LVH than in those without. Ca2+-ATPase mRNA levels in lambs with and without LVH and adult sheep without LVH were similar. Diastolic dysfunction occurred in the absence of subendomyocardial hypoperfusion, suggesting a nonischemic mechanism. In adult sheep with LVH diastolic dysfunction was associated with a marked reduction in Ca2+-ATPase mRNA levels.

L2 ANSWER 41 OF 41 SCISEARCH COPYRIGHT 2001 ISI (R)
AN 90:279423 SCISEARCH
GA The Genuine Article (R) Number: DD873
TI BASE CHANGES AT POSITION-792 OF ESCHERICHIA-COLI 16S RIBOSOMAL-RNA AFFECT ASSEMBLY OF 70S RIBOSOMES
AU SANTER M (Reprint); ***BENNETTGUERRERO E*** ; BYAHATTI S; CZARNECKI S; OCONNELL D; MEYER M; KHOURY J; CHENG X; SCHWARTZ I; MCLAUGHLIN J
CS HAVERFORD COLL, DEPT BIOL, HAVERFORD, PA, 19041 (Reprint); NEW YORK MED COLL, DEPT BIOCHEM & MOLEC BIOL, VALHALLA, NY, 10595
CYA USA
SO PROCEEDINGS OF THE NATIONAL ACADEMY OF SCIENCES OF THE UNITED STATES OF AMERICA, (1990) Vol. 87, No. 10, pp. 3700-3704.
DT Article; Journal
FS LIFE
LA ENGLISH
REC Reference Count: 32

=> e barclay george r/au
E1 39 BARCLAY GEORGE G/AU
E2 1 BARCLAY GEORGE GERARD/AU
E3 0 --> BARCLAY GEORGE R/AU
E4 3 BARCLAY GEORGE ROBIN/AU
E5 2 BARCLAY GERALD M/AU
E6 1 BARCLAY GILLIAN/AU
E7 1 BARCLAY GILPIN C/AU
E8 6 BARCLAY GLEN E/AU
E9 11 BARCLAY GORDON A/AU
E10 2 BARCLAY GRAEME J/AU
E11 1 BARCLAY GREGOR/AU
E12 2 BARCLAY GRIZEL R/AU

=> s e4
L3 3 "BARCLAY GEORGE ROBIN"/AU

=> dup rem l3
PROCESSING COMPLETED FOR L3
L4 3 DUP REM L3 (0 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 3 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 3 USPATFULL
AN 1999:4392 USPATFULL
TI Monoclonal antibody against LPS core
IN Gram, Hermann, Weil-Haltingen, Germany, Federal Republic of
Di Padova, Franco, Birsfelden, Switzerland
Barclay, George Robin , Midlothian, United Kingdom
Poxton, Ian Raymond, Midlothian, United Kingdom
PA Common Services Agency, United States (non-U.S. corporation)
PI US 5858728 19990112
AI US 1996-647144 19960509 (8)
RLI Continuation of Ser. No. US 1993-119046, filed on 30 Sep 1993, now abandoned
PRAI GB 1991-5292 19910313
DT Utility
FS Granted
EXNAM Primary Examiner: Loring, Susan A.
LREP Bell Seltzer Intellectual Property Law Group of Alston & Bird LLP
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 2426
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides monoclonal antibodies (Mabs) which are cross-protective against endotoxemia caused by at least two different Gram-negative bacterial strains having different core structures; and methods of production of these antibodies. By use of the Kohler/Milstein procedure involving immunization of mice with a number of different rough strains of heat-killed Gram-negative bacteria, followed by fusion and proper screening of the resulting hybridomas, such murine MAbs are obtained. The murine MAbs may be chimerized or humanized by known methods. For example, a chimeric MAb of IgG isotype is provided in which the hypervariable regions of the heavy chain have the amino acid sequences: Asp Tyr Tyr Met Thr; Leu Ile Arg Asn Lys Arg Asn Gly Asp Thr Ala Glu Tyr Ser Ala Ser Val Lys; and Gln Gly Arg Gly Tyr Thr Leu Asp Tyr; the hypervariable regions of the light chain have the amino acid sequences: Arg Ala Ser Gln Asn Ile Asn Ile Trp Leu Ser; Lys Ala Ser Asn Leu His Thr; and Leu Gln Gly Gln Ser Tyr Pro Arg Thr; the framework regions in the variable domains are murine and the constant domains are human.

L4 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 1998:761797 CAPLUS
DN 130:17217
TI Vaccine against lipopolysaccharide core
IN Bennett-Guerrero, Elliott; ***Barclay, George Robin*** ; Poxton, Ian Raymond; McIntosh, Thomas James; Snyder, David Scott
PA Medical Defense Technologies, Llc, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent

LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9851217	A1	19981119	WO 1998-US9988	19980515
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874912	A1	19981208	AU 1998-74912	19980515
EP 1011440	A1	20000628	EP 1998-922339	19980515
R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				

PRAI US 1997-46680 P 19970516
WO 1998-US9988 W 19980515

AB Complete core LPS (lacking O-polysaccharide side chains) from Gram-neg. bacteria are incorporated into a vaccine typically in liposomes. The complete core of E. coli K 12 is particularly useful. Upon administration to a mammal the vaccine stimulates synthesis of antibodies which are cross-protective against smooth and rough forms of LPS from at least two different Gram-neg. bacterial strains having different core structures.

RE.CNT 9
RE
(1) Dale, P; The Journal of Infectious Diseases 1992, V166, P316 CAPLUS
(2) Dipadova, F; Infection and Immunity 1993, V61(9), P3863 CAPLUS
(3) Fang, I; Infection and Immunity 1993, V61(9), P3873 CAPLUS
(4) Green, S; Advances in Experimental Medicine and Biology 1995, V383, P83 CAPLUS
(6) Poxton, I; Journal of Immunological Methods 1995, V186, P1 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 3 CAPLUS COPYRIGHT 2001 ACS
AN 1993:122974 CAPLUS
DN 118:122974
TI Monoclonal and humanized antibodies against the lipopolysaccharide core antigen of gram-negative bacteria
IN Gram, Hermann; Di Padova, Franco; ***Barclay, George Robin*** ; Poxton, Ian Raymond
PA Sandoz Ltd., Switz.; Sandoz-Patent-G.m.b.H.
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9216624	A1	19921001	WO 1992-EP380	19920222
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				

CA 2105979 AA 19920914 CA 1992-2105979 19920222
AU 9212611 A1 19921021 AU 1992-12611 19920222
EP 576439 A1 19940105 EP 1992-904901 19920222
EP 576439 B1 19990506
R: AT, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE
JP 06505867 T2 19940707 JP 1992-504918 19920222
AT 179753 E 19990515 AT 1992-904901 19920222
ES 2131526 T3 19990801 ES 1992-904901 19920222
US 5858728 A 19990112 US 1996-647144 19960509
PRAI GB 1991-5292 19910313
WO 1992-EP380 19920222
US 1993-119046 19930930
AB Antibodies that recognize the lipopolysaccharide of gram-neg. bacteria and so are useful in the treatment of gram-neg. bacteremia are prepd. and humanized antibodies are prepd. from them. Hybridomas were prepd. by std. methods using spleen cells from mice immunized with killed gram-neg. bacteria. The cDNAs encoding the variable regions were cloned by PCR using amino acid sequence-derived primers and these were ligated to human const. region cDNAs to generate humanized antibody cDNAs. Expression of the cDNAs for 2 such antibodies in SP2/0 cells is demonstrated.

=> e poxton ian r/au
E1 3 POXTON I R */AU
E2 5 POXTON IAN/AU
E3 65 --> POXTON IAN R/AU
E4 3 POXTON IAN RAYMOND/AU
E5 1 POXTON M/AU
E6 50 POXTON M G/AU
E7 2 POXTON MICHAEL G/AU
E8 1 POXTON R/AU
E9 1 POY A C/AU
E10 11 POY C/AU
E11 1 POY C D/AU
E12 1 POY CARLO/AU

=> s e1-e4
L5 76 ("POXTON I R *"/AU OR "POXTON IAN"/AU OR "POXTON IAN R"/AU OR "POXTON IAN RAYMOND"/AU)

=> dup rem l5
PROCESSING COMPLETED FOR L5
L6 57 DUP REM L5 (19 DUPLICATES REMOVED)

=> d bib ab 1-
YOU HAVE REQUESTED DATA FROM 57 ANSWERS - CONTINUE? Y/(N):y

L6 ANSWER 1 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2001:249647 BIOSIS
DN PREV200100249647
TI Mucosal and systemic antibody responses to the lipopolysaccharide of Escherichia coli O157 in health and disease.
AU Currie, Carol G.; McCallum, Kirsten; ***Poxton, Ian R. (1)***

CS (1) Department of Medical Microbiology, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG: i.r.poxton@ed.ac.uk UK
SO Journal of Medical Microbiology, (April, 2001) Vol. 50, No. 4, pp. 345-354. print.
ISSN: 0022-2615.
DT Article
LA English
SL English
AB Mucosal immunity in the gastrointestinal (GI) tract is a primary defence against GI pathogens. We hypothesise that a mucosal response to lipopolysaccharide (LPS), especially to the common (core) determinants of GI pathogenic Escherichia coli strains, is protective. The aims of this study were to investigate the specificities, levels and development of humoral responses in health and GI disease to the R3 LPS core and O-polysaccharide of E. coli O157. The purpose was to try to predict whether vaccination or passive immunisation might induce protection. Wherever possible, paired whole gut lavage fluid (WGLF) and serum samples were collected for comparison of the mucosal and systemic responses. Matched saliva samples were also collected from some study groups. The patient groups included those with acute E. coli O157 disease (serum only), patients convalescing after E. coli O157 infections, and patients undergoing routine investigation for GI conditions but subsequently shown to be immunologically normal. Some samples of WGLF from patients with Crohn's disease (CRO) and ulcerative colitis (UC) were included to allow comparisons with patients with inflammatory conditions known to alter antibody secretion in the GI tract. The healthy groups from whom serum and saliva only were taken included blood donors, healthy volunteers and a group of slaughterhouse workers. This latter group was likely to have been exposed regularly to faecal bacteria from animals and antibody specificities might have been expected to be different from other healthy individuals. Levels and classes of antibodies were determined by ELISA with microtitration plates coated with polymyxin complexes of whole LPS extracted from E. coli O157 and LPS from the E. coli R3 rough mutant. Antibodies of IgG and IgM classes were measured in serum and IgA was measured in WGLF and saliva. IgG antibodies to the O157 LPS and the R3 core oligosaccharide were detected in the serum of healthy blood donors. Patients with acute E. coli O157 disease showed elevated levels of serum IgM to O157 LPS and R3, with IgG levels raised only to R3. In serum from convalescent patients, IgG to O157 LPS was significantly above the control groups only in the period 6-16 weeks after infection. Total IgA levels were similar in WGLF specimens from all groups, except the patients with UC, whose levels were much higher. Specific IgA levels were higher in the E. coli O157 convalescent group, but there were no significant correlations overall. UC patients had significantly lower levels of IgA to O157 and CRO patients had higher O157 IgA levels than UC patients and healthy volunteers. In serum, inhibition of ELISA showed that the response to the O157 LPS was due in part to a response to the R3 oligosaccharide component. This response was much more pronounced in the healthy and non-O157 groups than in convalescent patients. There was no correlation between specific IgA antibody levels in saliva and matched specimens of WGLF, and levels in sequential saliva specimens fluctuated widely. The significant IgG and IgA responses to the R3 core suggest that there is immunological memory to this oligosaccharide LPS component which may have a role in protection against E. coli LPS both systemically and locally in

the GI tract. Boosting of this mucosal response to the LPS core, either naturally through exposure or by active or passive immunisation, may confer protection. Finally, antibody responses to E. coli O157 must be interpreted with caution, as the response detected is a sum of responses to the O-specific polysaccharide and the R3 core.

L6 ANSWER 2 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 2001:281993 CAPLUS
TI Search for enterotoxin gene in Bacteroides fragilis strains isolated from clinical specimens in Poland, Great Britain, the Netherlands and France
AU Luczak, Miroslaw; Obuch-Woszczatynski, Piotr; Pituch, Hanna; Leszczynski, Piotr; Martirosian, Gayane; Patrick, Sheila; ***Poxton, Ian*** ; Wintermans, Rob G. F.; Dubreuil, Luc; Meisel-Mikolajczyk, Felicja
CS Department of Medical Microbiology, Center of Biostructure Research, Medical University of Warsaw, Warsaw, 02-004, Pol.
SO Med. Sci. Monit. (2001), 7(2), 222-225
CODEN: MSMOFR; ISSN: 1234-1010
PB Medical Science International Publishing
DT Journal
LA English
AB Background: Bacteroides fragilis is a member of normal human flora and well known pathogenic agent. This bacterium produces many virulence factors. In 1984 new virulence factor - enterotoxin was described. The aim of the study was to search for enterotoxin gene in B. fragilis strains isolated from clin. specimens. Material and Methods: Strains isolated in Poland, Great Britain, France and the Netherlands were cultured on BBE medium. For DNA isolation Genomic DNA PREP PLUS isolation kit manufd. by A&A Biotechnol. (Poland) was used. In order to detect enterotoxin (fragilysin) gene, polymerase chain reaction (PCR) was applied utilizing the following primers: 404 (GAG CGG AAG ACG GTG TAT GTG ATT TGT) and 407 (TGC TCA GCG CCC AGT ATA TGA CCT AGT). DNA obtained from bacterial cells was amplified in thermocycler Techne. The amplification products were detected by the electrophoresis in 1% agarose gel. Results: Among 65 investigated B. fragilis strains, the enterotoxin gene was detected in DNA isolated from 12 strains. Conclusion: The enterotoxin producing B. fragilis strains were detected among strains isolated from different clin. specimens in Poland, Great Britain, the Netherlands and France.
RE.CNT 31
RE
(1) Beckmann, I; Int J Biochem 1989, V21, P661 CAPLUS
(3) Delahooke, D; J Med Microbiol 1995, V42, P102 MEDLINE
(8) Meisel-Mikolajczyk, F; Acta Microbiol Polon 1980, V29, P125 CAPLUS
(22) Pantosti, A; J Med Microbiol 1994, V41, P191 CAPLUS
(30) Weikel, C; Infect Immun 1992, V60, P321 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 3 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
AN 2000:534435 BIOSIS
DN PREV200000534435
TI Preparation and preclinical evaluation of a novel liposomal complete-core lipopolysaccharide vaccine.
AU Bennett-Guerrero, Elliott (1); McIntosh, Thomas J.; Barclay, G. Robin; Snyder, D. Scott; Gibbs, Richard J.; Mythen, Michael G.; ***Poxton, Ian*** *** R.***

CS (1) Department of Anesthesiology, Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York, NY, 10032-3784 USA
SO Infection and Immunity, (November, 2000) Vol. 68, No. 11, pp. 6202-6208. print.
ISSN: 0019-9567.
DT Article
LA English
SL English
AB Our objective is to develop a prophylactic vaccine strategy that can be evaluated for surgical and other high-risk hospitalized patients. In this paper, we describe the preparation and preclinical evaluation of a liposomal complete-core lipopolysaccharide (LPS) vaccine that is nontoxic and broadly antigenic. Complete-core (Ra-chemotype) LPSs were isolated from four gram-negative bacterial strains (Escherichia coli K-12, E. coli R1, Pseudomonas aeruginosa PAC608, and Bacteroides fragilis), mixed together to form a cocktail of complete-core LPSs, and then incorporated into multilamellar liposomes consisting of dimyristoyl phosphatidyl choline, dimyristoyl phosphatidylglycerol, and cholesterol in a 4:1:4 molar ratio. The endotoxic activities of these LPS-containing liposomes were less than 0.1% of the endotoxicities of the original free LPSs as measured by the Limulus amoebocyte lysate assay. In vivo administration of liposomal complete-core LPS mixed with Al(OH)3 to rabbits resulted in no pyrogenicity or overt toxicity over a 7-day period. In immunoblots, sera from rabbits following active immunization elicited cross-reactive antibodies to a large panel of rough and smooth LPSs from numerous clinically relevant gram-negative bacteria, including E. coli (serotypes O1, O4, O6, O8, O12, O15, O18, O75, O86, O157, and O111), P. aeruginosa (Fisher-Devlin serotypes 1, 2, and 3, which correspond to International Antigenic Typing Scheme types 6, 11, and 2, respectively), Klebsiella pneumoniae (serotypes O1, O2ab, and O3), B. fragilis, and Bacteroides vulgatus. Active immunization of mice with liposomal complete-core LPS provided protection against a lethal challenge with E. coli O18 LPS. The vaccine tested was nontoxic, nonpyrogenic, and immunogenic against a wide variety of pathogens found in clinical settings.

L6 ANSWER 4 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
AN 2000:336448 BIOSIS
DN PREV200000336448
TI Endotoxin and nanobacteria in polycystic kidney disease.
AU Hjelle, J. Thomas (1); Miller-Hjelle, Marcia A.; ***Poxton, Ian R.*** ; Kajander, E. Olavi; Ciftcioglu, Neva; Jones, Monica L.; Caughey, Robert C.; Brown, Robert; Millikin, Paul D.; Darras, Frank S.
CS (1) Department of Biomedical and Therapeutic Sciences, University of Illinois College of Medicine at Peoria, Peoria, IL, 61656 USA
SO Kidney International, (June, 2000) Vol. 57, No. 6, pp. 2360-2374. print.
ISSN: 0085-2538.
DT Article
LA English
SL English
AB Background: Microbes have been suspected as provocateurs of polycystic kidney disease (PKD), but attempts to isolate viable organisms have failed. Bacterial endotoxin is the most often reported microbial product found in PKD fluids. We assessed potential microbial origins of endotoxin in cyst fluids from 13 PKD patients and urines of PKD and control

individuals. Methods: Fluids were probed for endotoxin and nanobacteria, a new bacterium, by the differential Limulus Amebocyte Lysate assay (dLAL), genus-specific antilipopolysaccharide (LPS) antibodies, monoclonal antibodies to nanobacteria, and hyperimmune serum to Bartonella henselae (HS-Bh). Selected specimens were also assessed by transmission electron microscopy (TEM) and nanobacterial culture methods. Results: LPS or its antigenic metabolites were found in more than 75% of cyst fluids tested. Nanobacteria were cultured from 11 of 13 PKD kidneys, visualized in 8 of 8 kidneys by TEM, and immunodetected in all 13 PKD kidneys. By immunodetection, nanobacterial antigens were found in urine from 7 of 7 PKD males, 1 of 7 PKD females, 3 of 10 normal males, and 1 of 10 normal females. "Nanobacterium sanguineum" was dLAL positive and cross-reactive with antichlamydial LPS and HS-Bh. Some cyst fluids were also positive for LPS antigens from Escherichia coli, Bacteroides fragilis and/or Chlamydia, and HS-Bh, as were liver cyst fluids from one patient. Tetracycline and citrate inhibited nanobacterial growth in vitro. Conclusion: Nanobacteria or its antigens were present in PKD kidney, liver, and urine. The identification of candidate microbial pathogens is the first step in ascertaining their contribution, if any, to human disease.

L6 ANSWER 5 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
AN 2000:193374 BIOSIS
DN PREV200000193374
TI Exposure to Bacteroides fragilis endotoxin during cardiac surgery.
AU Bennett-Guerrero, Elliott (1); Barclay, G. Robin; Youssef, Michael E.; Hossain, Sabera; Vela-Cantos, Frances; Andres, Lewis A.; ***Poxton, Ian*** *** R.***
CS (1) Department of Anesthesiology, Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York, NY, 10032-3784 USA
SO Anesthesia & Analgesia, (April, 2000) Vol. 90, No. 4, pp. 819-823. ISSN: 0003-2999.
DT Article
LA English
SL English
AB Although endotoxemia has been observed during cardiac surgery, the identity of endotoxins to which patients are exposed is unknown. We tested the hypothesis that antibodies to Bacteroides fragilis (an anaerobic gut commensal and a common pathogen) decrease during cardiac surgery, thereby reflecting systemic exposure to this type of endotoxin. Serum antiendotoxin antibody levels were measured in 55 patients during routine cardiac surgery at the following times: Preoperatively, Pre-CPB (immediately before initiation of cardiopulmonary bypass (CPB)), Pre-CPB+5 (5 min after initiation of CPB), and End (end of surgery). Antiendotoxin antibody levels were determined by using enzyme-linked immunosorbent assay. Total immunoglobulin M (IgM) levels were measured by using laser nephelometry and decreases in total IgM levels were used to control changes in antiendotoxin antibody levels attributable to hemodilution. Median (interquartile range) hemodilution corrected IgM anti-B fragilis antibody levels decreased by 12% (5%-20%) from Preoperatively to End of surgery ($P < 0.001$). In contrast, median hemodilution corrected anti-B fragilis antibody levels did not change significantly from Pre-CPB to Pre-CPB+5, validating the correction for hemodilution. Immunoglobulin G anti-B fragilis antibody levels and IgM and immunoglobulin G anticore antibody levels decreased similarly during surgery. Intraoperatively,

levels of anti-B fragilis endotoxin antibodies decreased significantly out of proportion to hemodilution. These results suggest that cardiac surgical patients are exposed to B fragilis endotoxin. Implications: We prospectively measured hemodilution-corrected antiendotoxin antibody levels in 55 cardiac surgical patients. We observed significant decreases in hemodilution-corrected levels of antibody to both Bacteroides fragilis and the core of endotoxin.

L6 ANSWER 6 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:542675 BIOSIS
DN PREV200000542675
TI The biological activity of a liposomal complete core LPS vaccine.
AU Erridge, Clett (1); Stewart, John (1); Bennett-Guerrero, Elliott; ***Poxton, Ian R. (1)***
CS (1) Department of Medical Microbiology, University of Edinburgh Medical School, Edinburgh UK
SO Journal of Endotoxin Research, (2000) Vol. 6, No. 2, pp. 133. print.
Meeting Info.: 6th Conference of the International Endotoxin Society Paris, France August 24-27, 2000
ISSN: 0968-0519.
DT Conference
LA English
SL English

L6 ANSWER 7 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:97395 BIOSIS
DN PREV200000097395
TI Endotoxic activity of lipopolysaccharides isolated from emergent potential cystic fibrosis pathogens.
AU Hutchison, Michael L.; Bonell, Emma C.; ***Poxton, Ian R.*** ; Govan, John R. W. (1)
CS (1) Department of Medical Microbiology, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SO FEMS Immunology and Medical Microbiology, (Jan., 2000) Vol. 27, No. 1, pp. 73-77.
ISSN: 0928-8244.
DT Article
LA English
SL English
AB Improved antimicrobial therapies against the classical spectrum of pathogenic bacteria which colonise the lungs of cystic fibrosis (CF) patients has resulted in improved life expectancy and quality of life. Bacterial species that are resistant to a broad range of antibiotics including Stenotrophomonas maltophilia and Alcaligenes xylosoxidans have now emerged as potential new pathogens to fill the niche. At present, it is unclear from clinical data whether these microbes are commensal or pathogenic. In this study we have quantified the inflammatory potential of lipopolysaccharide (LPS) from eight species of Gram-negative organisms which have been cultured with increasing frequency from CF patients. Inflammatory responses induced by LPS from whole human blood and a human-derived monocyte cell line (THP-1) were assessed. Enzyme-linked immunosorbent assays were used to detect interleukin-6, interleukin-8, and tumour necrosis factor alpha (TNF). A bioassay was also used to assess TNF activity. With the exception of S. maltophilia, LPS extracted from all of

the bacteria tested upregulated, by varying degrees, expression of each of the proinflammatory cytokines assayed. This study represents the first comprehensive report of the endotoxic potential of a new wave of microbes which are associated with CF.

L6 ANSWER 8 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:218986 BIOSIS
DN PREV200000218986
TI Gut mucosal humoral immunity against core types of LPS of E. coli: A potential novel approach of mucosally presented vaccine.
AU Hoque, S. S. (1); ***Poxton, Ian R.*** ; Ghosh, S. (1)
CS (1) GI Unit, Department of Medical Sciences, University of Edinburgh, Edinburgh UK
SO Gut, (April, 2000) Vol. 46, No. 11, pp. A69.
Meeting Info.: 2000 Annual Meeting of the British Society of Gastroenterology. Birmingham, UK March 21-23, 2000 British Society of Gastroenterology
. ISSN: 0017-5749.
DT Conference
LA English
SL English

L6 ANSWER 9 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:218985 BIOSIS
DN PREV200000218985
TI Differences in intestinal humoral immunity between healthy volunteers from UK and Bangladesh.
AU Hoque, S. S. (1); ***Poxton, Ian R.*** ; Ghosh, S. (1)
CS (1) GI Unit, Department of Medical Sciences, University of Edinburgh, Edinburgh UK
SO Gut, (April, 2000) Vol. 46, No. 11, pp. A69.
Meeting Info.: 2000 Annual Meeting of the British Society of Gastroenterology. Birmingham, UK March 21-23, 2000 British Society of Gastroenterology
. ISSN: 0017-5749.
DT Conference
LA English
SL English

L6 ANSWER 10 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:269537 BIOSIS
DN PREV200000269537
TI Gut bacteria and ulcerative colitis: A broken tolerance.
AU Hoque, Syed S. (1); ***Poxton, Ian R.*** ; Ghosh, Subrata
CS (1) GI Unit, Western Gen Hosp, Edinburgh UK
SO Gastroenterology, (April, 2000) Vol. 118, No. 4 Suppl. 2 Part 1, pp. AGA A807. print..
Meeting Info.: 101st Annual Meeting of the American Gastroenterological Association and the Digestive Disease Week. San Diego, California, USA May 21-24, 2000 American Gastroenterological Association
. ISSN: 0016-5085.
DT Conference
LA English
SL English

L6 ANSWER 11 OF 57 USPATFULL
AN 1999:4392 USPATFULL
TI Monoclonal antibody against LPS core
IN Gram, Hermann, Weil-Haltingen, Germany, Federal Republic of
Di Padova, Franco, Birsfelden, Switzerland
Barclay, George Robin, Midlothian, United Kingdom
Poxton, Ian Raymond , Midlothian, United Kingdom
PA Common Services Agency, United States (non-U.S. corporation)
PI US 5858728 19990112
AI US 1996-647144 19960509 (8)
RLI Continuation of Ser. No. US 1993-119046, filed on 30 Sep 1993, now abandoned
PRAI GB 1991-5292 19910313
DT Utility
FS Granted
EXNAM Primary Examiner: Loring, Susan A.
LREP Bell Seltzer Intellectual Property Law Group of Alston & Bird LLP
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 2426
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides monoclonal antibodies (Mabs) which are cross-protective against endotoxemia caused by at least two different Gram-negative bacterial strains having different core structures; and methods of production of these antibodies. By use of the Kohler/Milstein procedure involving immunization of mice with a number of different rough strains of heat-killed Gram-negative bacteria, followed by fusion and proper screening of the resulting hybridomas, such murine MAbs are obtained. The murine MAbs may be chimerized or humanized by known methods. For example, a chimeric MAb of IgG isotype is provided in which the hypervariable regions of the heavy chain have the amino acid sequences: Asp Tyr Tyr Met Thr; Leu Ile Arg Asn Lys Arg Asn Gly Asp Thr Ala Glu Tyr Ser Ala Ser Val Lys; and Gln Gly Arg Gly Tyr Thr Leu Asp Tyr; the hypervariable regions of the light chain have the amino acid sequences: Arg Ala Ser Gln Asn Ile Asn Ile Trp Leu Ser; Lys Ala Ser Asn Leu His Thr; and Leu Gln Gly Gln Ser Tyr Pro Arg Thr; the framework regions in the variable domains are murine and the constant domains are human.

L6 ANSWER 12 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
AN 1999:435032 BIOSIS
DN PREV199900435032
TI Lipopolysaccharide chemotypes of Burkholderia cepacia.
AU Evans, Elwyn; ***Poxton, Ian R. (1)*** ; Govan, John R. W.
CS (1) Department of Medical Microbiology, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SO Journal of Medical Microbiology, (Sept., 1999) Vol. 48, No. 9, pp. 825-832.
ISSN: 0022-2615.
DT Article
LA English
SL English

AB Burkholderia cepacia is an important pathogen in patients with cystic fibrosis (CF) and much is now known of its epidemiology. In contrast, its virulence mechanisms are poorly understood. The lipopolysaccharide (LPS) of B. cepacia, a well-recognised virulence factor of other gram-negative bacteria, is known to be strongly endotoxic in vitro. The aim of this study was to observe if there were any links between the structure of B. cepacia LPS and virulence. This has been investigated by polyacrylamide gel electrophoresis and immunoblotting to define the chemotype and antigenic cross reactivity of B. cepacia LPS. Strains (16) belonging to different genomovars of the B. cepacia complex were selected to represent epidemic and non-epidemic clinical isolates and environmental strains. All strains belonging to genomovars I and II (the latter now renamed B. multivorans) had smooth LPS. However, isolates belonging to genomovar III, the group to which most of the epidemic CF isolatesbelong - including the highly transmissible strain (ET 12) which has been found in both the UK and North America 11 - were of either rough or smooth LPS chemotype. In this study, B. cepacia J2315 represents the ET 12 lineage, and has a rough chemotype. Rabbit antiserum raised to strain J2315 revealed that the LPS core of this strain was antigenically related to some but not all other genomovar III strains, but it also cross-reacted strongly with all B. multivorans (genomovar II) and most genomovar I strains. Intra-strain phenotypic variation was demonstrated between bacteria grown in broth or on solid agar with a concomitant variation in antigenic cross reactivity. There was no clear evidence to associate any particular LPS phenotype with epidemic or non-epidemic strains, but changes in phenotype in vitro may provide clues to the survival and adaptability of B. cepacia in hostile environments and possibly to its ability to produce an inflammatory response in vivo.

L6 ANSWER 13 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:193157 BIOSIS
DN PREV200000193157
TI Is equine grass sickness (Mal Seco?) a form of botulism.
AU ***Poxton, Ian R. (1)*** ; Hunter, Leonie; Lough, Hannah; Miller, Keith
CS (1) Department of Medical Microbiology, University of Edinburgh Medical School, Edinburgh UK
SO Anaerobe, (June Aug., 1999) Vol. 5, No. 3-4, pp. 291-293.
ISSN: 1075-9964.
DT Article
LA English
SL English

L6 ANSWER 14 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AN 2000:190684 BIOSIS
DN PREV200000190684
TI Variation in the cell surface proteins of Clostridium difficile.
AU ***Poxton, Ian R. (1)*** ; Higgins, Paul G.; Currie, Carol G.; McCoubrey, Jodie
CS (1) Department of Medical Microbiology, University of Edinburgh Medical School, Edinburgh UK
SO Anaerobe, (June Aug., 1999) Vol. 5, No. 3-4, pp. 213-215.
ISSN: 1075-9964.
DT Conference
LA English

SL English

L6 ANSWER 15 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
AN 1999:263034 BIOSIS
DN PREV199900263034
TI The lipopolysaccharide core type of Escherichia coli O157:H7 and other non-O157 verotoxin-producing E. coli.
AU Currie, Carol G.; ***Poxton, Ian R. (1)***
CS (1) Department of Medical Microbiology, University of Edinburgh Medical School, Teviot Place, Edinburgh, EH8 9AG UK
SO FEMS Immunology and Medical Microbiology, (May, 1999) Vol. 24, No. 1, pp. 57-62.
ISSN: 0928-8244.
DT Article
LA English
SL English
AB A mouse monoclonal antibody specific for the R3 lipopolysaccharide core type of Escherichia coli was used to determine the core type of E. coli O157:H7 and other non-O157 verotoxin-producing E. coli strains. Lipopolysaccharide extracts from 28 clinical isolates were examined by sodium dodecylsulfate-polyacrylamide gel electrophoresis and immunoblotting and all were found to have the R3 core. None of the core lipopolysaccharide from the strains tested reacted with the control R1 and R2 specific monoclonal antibodies. A common core type between all the verotoxin-producing E. coli strains tested may be significant when considering the immune response to these bacteria, and to the receptor for the VT bacteriophage.

L6 ANSWER 16 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:384099 BIOSIS
DN PREV199900384099
TI Comparison of tissue factor induction in monocytes by different lipopolysaccharides.
AU McIlroy, Justine M. (1); Stirling, David (1); ***Poxton, Ian R.*** ; Ludlam, Christopher A. (1)
CS (1) Dept Haematology, University of Edinburgh, Royal Infirmary of Edinburgh, Edinburgh UK
SO British Journal of Haematology, (April, 1999) Vol. 105, No. SUPPL. 1, pp. 41.
Meeting Info.: Annual Scientific Meeting of the British Society for Haematology Brighton, England, UK April 12-15, 1999 British Society for Haematology
. ISSN: 0007-1048.
DT Conference
LA English

L6 ANSWER 17 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1998:761797 CAPLUS
DN 130:17217
TI Vaccine against lipopolysaccharide core
IN Bennett-Guerrero, Elliott; Barclay, George Robin; ***Poxton, Ian*** *** Raymond*** ; McIntosh, Thomas James; Snyder, David Scott
PA Medical Defense Technologies, Llc, USA
SO PCT Int. Appl., 51 pp.

CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9851217	A1	19981119	WO 1998-US9988	19980515
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874912	A1	19981208	AU 1998-74912	19980515
EP 1011440	A1	20000628	EP 1998-922339	19980515
R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				

PRAI US 1997-46680 P 19970516
WO 1998-US9988 W 19980515
AB Complete core LPS (lacking O-polysaccharide side chains) from Gram-neg. bacteria are incorporated into a vaccine typically in liposomes. The complete core of E. coli K 12 is particularly useful. Upon administration to a mammal the vaccine stimulates synthesis of antibodies which are cross-protective against smooth and rough forms of LPS from at least two different Gram-neg. bacterial strains having different core structures.
RE.CNT 9
RE
(1) Dale, P; The Journal of Infectious Diseases 1992, V166, P316 CAPLUS
(2) Dipadova, F; Infection and Immunity 1993, V61(9), P3863 CAPLUS
(3) Fang, I; Infection and Immunity 1993, V61(9), P3873 CAPLUS
(4) Green, S; Advances in Experimental Medicine and Biology 1995, V383, P83 CAPLUS
(6) Poxton, I; Journal of Immunological Methods 1995, V186, P1 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L6 ANSWER 18 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 8
AN 1998:258255 BIOSIS
DN PREV199800258255
TI Burkholderia cepacia produces a hemolysin that is capable of inducing apoptosis and degranulation of mammalian phagocytes.
AU Hutchison, Michael L. (1); ***Poxton, Ian R.*** ; Govan, John R. W.
CS (1) Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SO Infection and Immunity, (May, 1998) Vol. 66, No. 5, pp. 2033-2039. ISSN: 0019-9567.
DT Article
LA English
AB Burkholderia cepacia is an opportunistic pathogen that has become a major threat to individuals with cystic fibrosis (CF). In approximately 20% of patients, pulmonary colonization with B. cepacia leads to cepacia syndrome, a fatal fulminating pneumonia sometimes associated with septicemia. It has been reported that culture filtrates of clinically derived strains of B. cepacia are hemolytic. In this study, we have

characterized a factor which contributes to this hemolytic activity and is secreted from B. cepacia J2315, a representative of the virulent and highly transmissible strain belonging to the recently described genomovar III grouping. Biochemical data from the described purification method for this hemolysin allows us to hypothesize that the toxin is a lipopeptide. As demonstrated for other lipopeptide toxins, the hemolysin from B. cepacia was surface active and lowered the surface tension of high-pressure liquid chromatography-grade water from 12.96 to 29.8 mN m-1. Similar to reports for other pore-forming cytotoxins, low concentrations of the hemolysin were able to induce nucleosomal degradation consistent with apoptosis in human neutrophils and the mouse-derived macrophage-type cell line J774.2. Exposure of human neutrophils to higher concentrations of toxin resulted in increased activities of the neutrophil degranulation markers cathepsin G and elastase. Based on the results obtained in this study, we suggest a role that allows B. cepacia to thwart the immune response and a model of the events that may contribute to the severe inflammatory response in the lungs of CF patients.

L6 ANSWER 19 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 9
AN 1998:364146 BIOSIS
DN PREV199800364146
TI Differential effects of bacterial lipopolysaccharides upon neutrophil function.
AU Ruchaud-Sparagano, Marie-Helene (1); Riuvenkamp, Claudia A.; Riches, Philip L.; ***Poxton, Ian R.*** ; Dransfield, Ian
CS (1) Rayne Lab., Respiratory Med. Unit, Univ. Edinburgh Med. Sch., Teviot Pl., Edinburgh EH8 9AG UK
SO FEBS Letters, (July 3, 1998) Vol. 430, No. 3, pp. 363-369. ISSN: 0014-5793.
DT Article
LA English
AB Lipopolysaccharide (LPS) is a potent inflammatory agent which augments neutrophil sensitivity to subsequent inflammatory stimuli. In this study, the effects of structurally different LPS types upon neutrophil effector functions were examined. Rough LPS types, which have lost the O-polysaccharide moiety, were found to act more rapidly than smooth LPS types in stimulating neutrophil beta2 integrin activity and fMLP-induced respiratory burst. These findings suggest an involvement of the O-polysaccharide region of LPS in regulating neutrophil responsiveness to different LPS chemotypes with important implications for the mechanisms underlying regulation of the inflammatory response in conditions associated with elevation of LPS in plasma, e.g., septic shock or acute respiratory distress syndrome.

L6 ANSWER 20 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1998:566293 CAPLUS
TI Towards anti-adhesion therapy for microbial diseases I. Kahane and I. Ofek, eds.
AU ***Poxton, Ian R.***
CS Department of Medical Microbiology, Medical School, University of Edinburgh, Edinburgh, EH8 9AG, UK
SO J. Antimicrob. Chemother. (1998), 42(2), 285-286 CODEN: JACHDX; ISSN: 0305-7453
PB Oxford University Press

DT Journal; Book Review
LA English
AB Unavailable

L6 ANSWER 21 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 10
AN 1997:221921 BIOSIS
DN PREV199799513637
TI Isolation of a cell surface component of Helicobacter pylori that binds H type 2, Lewis-a, and Lewis-b antigens.
AU Alkout, Abdulhamid M.; Blackwell, C. Caroline (1); Weir, Donald M.; ***Poxton, Ian R.*** ; Elton, Robert A.; Luman, Widjaja; Palmer, Kelvin
CS (1) Dep. Med. Microbiol., Univ. Edinburgh, Teviot Place, Edinburgh EH8 9AG UK
SO Gastroenterology, (1997) Vol. 112, No. 4, pp. 1179-1187.
ISSN: 0016-5085.
DT Article
LA English
AB Background & Aims: Individuals of blood group O and nonsecretors of ABO blood group antigens are more susceptible to peptic ulcers. The aim of this study was to determine if blood group antigens associated with group O or secretor status are epithelial cell receptors for Helicobacter pylori. Methods: Bacterial binding and binding of monoclonal antibodies to H type 2, Lewis-a, and Lewis-b to Kato III, buccal epithelial, and gastric mucosal cells were shown by flow cytometry. Bacterial outer membrane proteins eluted from H type 2, Lewis-a, or Lewis-b were shown by polyacrylamide gel electrophoresis. Results: Kato III and human epithelial cells bound each monoclonal antibody; O cells bound more anti-H type 2 (P lt 0.05). Binding indices for H. pylori correlated with those for anti-H type 2 (P lt 0.005) and antiLewis-b (p lt 0.001) but not anti-Lewis-a. A 61-kilodalton protein was eluted from H type 2, Lewis-a, or Lewis-b. Conclusions: Our results indicate that H type 2 is an important receptor for the 61-kilodalton bacterial adhesin, partly explaining increased susceptibility of individuals of blood group O to ulcers. Lewis-b binds H. pylori more efficiently than Lewis-a. If these interactions occur in vivo, lack of Lewis-b in mucosal fluids of nonsecretors may contribute to colonization by H. pylori.

L6 ANSWER 22 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1997:481793 BIOSIS
DN PREV199799780996
TI The mucosal anaerobic gram-negative bacteria of the human colon.
AU ***Poxton, Ian R. (1)*** ; Brown, Robert; Sawyerr, Af; Ferguson, Anne
CS (1) Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SO Clinical Infectious Diseases, (1997) Vol. 25, No. SUPPL. 2, pp. S111-S113.
ISSN: 1058-4838.
DT General Review
LA English

L6 ANSWER 23 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:294069 BIOSIS
DN PREV199699016425
TI Monoclonal antibodies to endotoxin core as a new approach in endotoxemia therapy.

AU Di Padova, Franco (1); Gram, Hermann (1); Barclay, G. Robin; ***Poxton,*** *** Ian R.*** ; Liehl, Ekke; Rietschel, Ernst T.
CS (1) Sandoz Pharma, Basel Switzerland
SO Morrison, D. C. [Editor]; Ryan, J. L. [Editor]. Infectious Disease and Therapy, (1996) Vol. 19, pp. 13-31. Infectious Disease and Therapy; Novel therapeutic strategies in the treatment of sepsis.
Publisher: Marcel Dekker, Inc. 270 Madison Avenue, New York, New York 10016, USA.
ISSN: 1043-2981. ISBN: 0-8247-9661-6.
DT Book
LA English

L6 ANSWER 24 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1996:261861 CAPLUS
DN 124:340491
TI Monoclonal antibodies to endotoxin core as a new approach in endotoxemia therapy
AU Di Padova, Franco; Gram, Hermann; Barclay, G. Robin; ***Poxton, Ian*** *** R.*** ; Liehl, Ekke; Rietschel, Ernst th.
CS Sandoz Pharma, Basel, Switz.
SO Infect. Dis. Ther. (1996), 19(Novel Therapeutic Strategies in the Treatment of Sepsis), 13-31
CODEN: IDTHER; ISSN: 1043-2981
DT Journal
LA English
AB Rough mutants of E. coli strains which expressed the complete core glycolipid and different immunization protocols were used to produce cross-reactive and cross-neutralizing monoclonal antibodies to the core. This makes is possible to test the concept that these antibodies might be beneficial in patients with endotoxemia and sepsis.

L6 ANSWER 25 OF 57 LIFESCI COPYRIGHT 2001 CSA
AN 95:53794 LIFESCI
TI Tumor necrosis factor induction by an aqueous phenol-extracted lipopolysaccharide complex from Bacteroides species
AU Delahooke, D.M.; Barclay, G.R.; ***Poxton, I.R.****
CS Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG, Scotland, UK
SO INFECT. IMMUN., (1995) vol. 63, no. 3, pp. 840-846.
ISSN: 0019-9567.
DT Journal
FS J
LA English
SL English
AB The stimulation of macrophages and monocytes by lipopolysaccharide (LPS) results in the secretion of tumor necrosis factor (TNF), a cytokine which is thought to play a pivotal role in subsequent host responses. Its induction is thought to be facilitated by the binding of complexes of LPS and LPS-binding protein to CD14. The LPS of Bacteroides species was considered a weak endotoxin; however, in a recent study we have shown that the biological activity and chemical composition of the LPS from Bacteroides species are dependent on the extraction method. The present study determines the capacity of LPS extracted by aqueous phenol (the method for producing an LPS of high endotoxic activity) from four species

of Bacteroides to induce TNF. Induction was investigated from human mononuclear leukocytes (MNL), THP-1 cells (with and without enhancement by vitamin D sub(3) for CD14), and peritoneal macrophages from C3H/HeJ (LPS nonresponder) and C3H/HeN (LPS responder) mice. Escherichia coli O18K super(-) LPS, a typical smooth LPS of heterogeneous molecular mass, was used as a control throughout. The stimulation of TNF production by E. coli LPS was between two- and fourfold more than that by Bacteroides LPS in MNL, in THP-1 cells (with enhancement for CD14), and in peritoneal macrophages from C3H/HeN mice. In THP-1 cells (without enhancement for CD14), there was no significant difference in TNF production between E. coli and Bacteroides LPSs. In peritoneal macrophages from C3H/HeJ mice, E. coli LPS stimulated no TNF production, but there was no significant difference in TNF production from peritoneal macrophages from C3H/HeJ and C3H/HeN mice by Bacteroides LPS. In all cell populations, there was a peak of TNF production after approximately 4 h of stimulation with all LPSs tested. However, other peaks of TNF production were seen in MNL and THP-1 cells (with enhancement for CD14) after stimulation with E. coli LPS only. In stimulation assays in which Bacteroides LPS was together with but in excess of E. coli LPS, it was found that TNF production from MNL and THP-1 cells (with and without enhancement for CD14) was comparable to that of Bacteroides LPS alone and not E. coli LPS alone. An anti-CD14 monoclonal antibody did not inhibit Bacteroides LPS-stimulated TNF production. However, E. coli LPS-stimulated release was inhibited by an anti-CD14 monoclonal antibody, most noticeably in MNL and THP-1 cells (with enhancement for CD14). We conclude that Bacteroides LPS can mask the effects of E. coli LPS when present in excess, can produce only one peak of TNF production, and activates mononuclear cells by a pathway not dependent on CD14.

L6 ANSWER 26 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 11
AN 1995:392736 BIOSIS
DN PREV199598407036
TI Prophylactic use of human endotoxin-core hyperimmune gammaglobulin to prevent endotoxaemia in colostrum-deprived gnotobiotic lambs challenged orally with Escherichia coli.
AU Hodgson, J. Christopher (1); Barclay, G. Robin; Hay, Lorna A.; Moon, Gordon M.; ***Poxton, Ian R.***
CS (1) Moredun Res. Inst., 408 Gilmerton Rd., Edinburgh EH17 7JH UK
SO FEMS Immunology and Medical Microbiology, (1995) Vol. 11, No. 3, pp. 171-180.
ISSN: 0928-8244.
DT Article
LA English
AB The efficacy of human IgG polyclonal antibody to endotoxin-core in preventing endotoxemia and subsequent disease was studied in colostrum-deprived gnotobiotic lambs challenged orally at about 5 h old with 10-9 cfu Escherichia coli. Human endotoxin-core hyperimmune gammaglobulin was given intravenously to 5 lambs at 1.9 g IgG/kg bodyweight prior to challenge. Human albumin was given intravenously to 3 control lambs. Bacteremia was observed in all lambs, but the incidence was lower (P lt 0.01) and the onset later (P lt 0.05) in gammaglobulin pre-treated lambs. These lambs showed no signs of disease, whereas clinical endotoxemia, manifesting as watery mouth disease, was diagnosed in 2 of the 3 control lambs which were killed between 18 and 22 h after

challenge. Thus, prophylactic treatment of colostrum-deprived lambs with human IgG enriched in endotoxin-core antibodies was effective in reducing the degree of bacteremia and preventing endotoxemia, leukopenia and clinical disease following oral challenge with E. coli.

L6 ANSWER 27 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 12
AN 1995:339503 BIOSIS
DN PREV199598353803
TI Biological activity of Bacteroides lipopolysaccharide-reappraisal.
AU ***Poxton, Ian R. (1)*** ; Edmond, Diane M.
CS (1) Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SO Clinical Infectious Diseases, (1995) Vol. 20, No. SUPPL. 2, pp. S149-S153.
Meeting Info.: Proceedings of the 1994 Meeting of the Anaerobe Society of the Americas Marina del Rey, California, USA July 29-31, 1994
ISSN: 1058-4838.
DT Conference
LA English

L6 ANSWER 28 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 13
AN 1995:315840 BIOSIS
DN PREV199598330140
TI Biological activity of Burkholderia (Pseudomonas) cepacia lipopolysaccharide.
AU Shaw, Deborah; ***Poxton, Ian R.*** ; Govan, John R. W. (1)
CS (1) Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SO FEMS Immunology and Medical Microbiology, (1995) Vol. 11, No. 2, pp. 99-106.
ISSN: 0928-8244.
DT Article
LA English
AB Burkholderia cepacia has emerged as an important multiresistant pathogen in cystic fibrosis (CF), associated in 20% of colonised patients with a rapid and fatal decline in lung function. Although knowledge of B. cepacia epidemiology has improved, the mechanisms involved in pathogenesis remain obscure. In this study, B. cepacia lipopolysaccharide (LPS) was assessed for endotoxic potential and the capacity to induce tumour necrosis factor (TNF). LPS preparations from clinical and environmental isolates of B. cepacia and from the closely related species Burkholderia gladioli exhibited a higher endotoxic activity and more pronounced cytokine response in vitro compared to preparations from the major CF pathogen Pseudomonas aeruginosa. This study may help to explain the vicious host immune response observed during pulmonary exacerbations in CF patients colonised by B. cepacia and lead to therapeutic advances in clinical management.

L6 ANSWER 29 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 14
AN 1996:133252 BIOSIS
DN PREV199698705387
TI Clinical investigation of gut immune responses.
AU Ferguson, Anne (1); Sallam, Jamal; O'Mahony, Seamus; ***Poxton, Ian***
CS (1) Univ. Edinburgh Dep. Med., West. Gen. Hosp., Edinburgh EH14 2XU UK
SO Advanced Drug Delivery Reviews, (1995) Vol. 18, No. 1, pp. 53-71.

ISSN: 0169-409X.
DT General Review
LA English

L6 ANSWER 30 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 15
AN 1995:253201 BIOSIS
DN PREV199598267501
TI Anti-bacteroides lipopolysaccharide IgG levels in healthy adults and sepsis patients.
AU Allan, Elizabeth; ***Poxton, Ian R. (1)*** ; Barclay, G. Robin
CS (1) Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SO FEMS Immunology and Medical Microbiology, (1995) Vol. 11, No. 1, pp. 5-12.
DT Article
LA English
AB Members of the genus Bacteroides greatly outnumber enterobacteria in the human colon and therefore represent a vast potential pool of biologically active LPS. An enzyme-linked immunosorbent assay was developed to estimate the distribution of IgG levels to LPS from B. fragilis, B. vulgatus, B. thetaiotaomicron and to a mixture of rough LPS from three enterobacteria and Pseudomonas aeruginosa in sera from 641 adult blood donors. By inhibition ELISA some cross-reactivity was demonstrated between the different anti-bacteroides LPS IgG, but with very little between the anti-bacteroides LPS IgG and the anti-enterobacterial/Pseudomonas LPS IgG. Serum IgG was measured daily over 5-9-day periods in 12 sepsis patients (6 survivors, 6 non-survivors) and in a healthy individual. In all patients IgG levels fluctuated to a greater extent than levels in a healthy subject. Variations all followed similar overall trends and indicated that exposure to bacteroides LPS had occurred. In 5 out of 6 survivors, IgG levels were rising at the end of the period, while 4 of the 6 non-survivors showed falls, with an exception showing increasing levels to B. fragilis LPS. In 5 out of 6 non-survivors, IgG levels against B. fragilis LPS were substantially higher than those against the other LPSs. In this small sample some trends in antibody kinetics have been recognised which suggest bacteroides LPS may be significant in sepsis, and indicate that this study should be extended.

L6 ANSWER 31 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 16
AN 1995:548930 BIOSIS
DN PREV199698563230
TI Antibodies to lipopolysaccharide.
AU ***Poxton, Ian R.***
CS Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SO Journal of Immunological Methods, (1995) Vol. 186, No. 1, pp. 1-15.
ISSN: 0022-1759.
DT General Review
LA English
AB Lipopolysaccharides (LPS) are indispensable structural components of the Gram-negative bacterial outer membrane and are major determinants of virulence in pathogenic species. In the infected host LPS is better known as endotoxin where it acts as a potent stimulator of the inflammatory response. This article reviews the methods for the production and measurement of anti-LPS antibodies, and then describes the uses to which

these methods have been employed. Antibodies to LPS (either monoclonal or polyclonal) may be used directly as immunotherapeutic agents for the treatment of Gram-negative sepsis or endotoxaemia, or as probes for the diagnosis and epidemiological investigation of Gram-negative bacterial infections. Antibodies are useful tools for investigation of the chemical structure of LPS, its expression on bacteria and to study the role of LPS in pathogenic mechanisms. The detection and quantitation of anti-LPS antibodies has formed the basis of classical and more recent serological studies of major bacterial infections.

L6 ANSWER 32 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:424254 BIOSIS
DN PREV199497437254
TI Anti-lipopolysaccharide core antibodies.
AU Di Padova, Franco E. (1); Mikol, Vincent; Barclay, G. Robin; ***Poxton,*** *** Ian R.*** ; Brade, Helmut; Rietschel, Ernst T.
CS (1) Preclinical Res., Sandoz Pharma Ltd., CH-4002 Basel Switzerland
SO Levin, J. [Editor]; van Deventer, S. J. H. [Editor]; van der Poll, T. [Editor]; Sturk, A. [Editor]. Progress in Clinical and Biological Research, (1994) Vol. 388, pp. 85-94. Progress in Clinical and Biological Research; Bacterial endotoxins: Basic science to anti-sepsis strategies.
Publisher: Wiley-Liss, Inc. 605 Third Avenue, New York, New York 10158-0012, USA.
Meeting Info.: Fourth International Conference on Endotoxins Amsterdam, Netherlands August 1993
ISSN: 0361-7742. ISBN: 0-471-02181-4.
DT Book; Conference
LA English

L6 ANSWER 33 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:371136 BIOSIS
DN PREV199497384136
TI The gut as an immune organ: Intestinal antiendotoxin antibodies.
AU Ferguson, Anne (1); Sallam, Jamal; McLintock, Laura; Croft, Nicholas; ***Poxton, Ian***
CS (1) Dep. Med., Univ. Edinburgh, Western General Hosp., Edinburgh EH4 2XU UK
SO Kinney, J. M. [Editor]; Tucker, H. N. [Editor]. (1994) pp. 231-244. Organ metabolism and nutrition: Ideas for future critical care.
Publisher: Raven Press 1185 Avenue of the Americas, New York, New York 10036-2806, USA.
Meeting Info.: Second Clintec International Horizons Conference Amsterdam, Netherlands May 16-20, 1993
ISBN: 0-7817-0160-0.
DT Book; Conference
LA English

L6 ANSWER 34 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 17
AN 1994:316412 BIOSIS
DN PREV199497329412
TI Isolation of an adhesin from Staphylococcus aureus that binds Lewis-a blood group antigen and its relevance to sudden infant death syndrome.
AU Saadi, Abdulrahman T.; Weir, Donald M.; ***Poxton, Ian R.*** ; Stewart, John; Essery, Steven D.; Blackwell, C. Caroline (1); Raza, Mohammed W.;

Busuttil, Anthony
CS (1) Dep. Med. Microbiol., Univ. Edinburgh, Med. Sch., Teviot Place, Edinburgh EH8 9AG UK
SO FEMS Immunology and Medical Microbiology, (1994) Vol. 8, No. 4, pp. 315-320.
DT Article
LA English
AB A 67 kDa protein was isolated from cell membrane preparations of Staphylococcus aureus (NCTC 10655) by affinity adsorption with synthetic Lewis-a antigen conjugated to Synsorb beads. Pre-treatment of buccal epithelial cells expressing Lewis a with the purified protein reduced binding of the staphylococcal strain to a greater extent than the material not bound to the Synsorb beads. The significance of this work is discussed with reference to expression of Lewis-a antigen in infants and the proposed role of toxigenic strains of staphylococci in some cases of sudden infant death syndrome.

L6 ANSWER 35 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:315415 BIOSIS
DN PREV199497328415
TI Serum sensitivity of Burkholderia (Pseudomonas) cepacia isolates from patients with cystic fibrosis.
AU Butler, Sarah L. (1); Nelson, James W.; ***Poxton, Ian R.*** ; Govan, John R. W.
CS (1) Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot PlaCe, Edinburgh EH8 9AG UK
SO FEMS Immunology and Medical Microbiology, (1994) Vol. 8, No. 4, pp. 285-292.
DT Article
LA English
AB Bacterial strains which are sensitive to the bactericidal activity of serum are generally considered to be less virulent than serum-resistant strains and are seldom associated with bacteremia. Burkholderia (Pseudomonas) cepacia is an important pathogen in cystic fibrosis and is associated with rapid fatal pulmonary decline and bacteremia in 20% of colonized patients. In this study 19 isolates of B. cepacia expressing either rough or smooth LPS were investigated to determine the degree of serum sensitivity. Strains expressing rough-LPS were serum-sensitive: these included a highly transmissible strain of B. cepacia isolated from approximately 50 cystic fibrosis patients attending various U.K. regional centers and associated with cases of bacteremia.

L6 ANSWER 36 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1994:506105 CAPLUS
DN 121:106105
TI The gut as an immune organ: intestinal antiendotoxin antibodies
AU Ferguson, Anne; Sallam, Jamal; McLintock, Laura; Croft, Nicholas; ***Poxton, Ian***
CS Department of Medicine, University of Edinburgh, Edinburgh, EH4 2XU, UK
SO Organ Metab. Nutr. [Clintec Int. Horiz. Conf.], 2nd (1994), Meeting Date 1993, 231-44. Editor(s): Kinney, John M.; Tucker, Hugh N. Publisher: Raven, New York, N. Y.
CODEN: 60GUAW
DT Conference; General Review

LA English
AB A review and discussion with 17 refs. Methods for safe and noninvasive examn. of gut mucosal immunity are available, based either on use of jejunal fluid or on whole gut lavage fluid. A new disease entity, intestinal IgA deficiency is discussed.

L6 ANSWER 37 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1995:134997 CAPLUS
DN 122:7484
TI Anti-lipopolysaccharide core antibodies
AU Padova, Franco E. Di; Mikol, Vincent; Barclay, G. Robin; ***Poxton, Ian*** *** R.*** ; Brade, Helmut; Rietschel, Ernst T.
CS Preclinical Research, Sandoz Pharma Ltd, Basel, CH-4002, Switz.
SO Prog. Clin. Biol. Res. (1994), 388(BACTERIAL ENDOTOXINS), 85-94 CODEN: PCBRD2; ISSN: 0361-7742
DT Journal
LA English
AB A murine monoclonal IgG2a antibody, WN 222-5, which reacts with smooth and rough forms of lipopolysaccharide, was chimerized into a human IgG1k antibody, SDZ 219-800. SDZ 219-800 inhibited secretion of interleukin-6 by mononuclear cells in a dose-dependent manner. In immunoblots, SDZ 219-800 could specifically detect nanogram amts. of E. coli lipopolysaccharide and could distinguish S-form lipopolysaccharide from R-form lipopolysaccharide.

L6 ANSWER 38 OF 57 LIFESCI COPYRIGHT 2001 CSA
AN 95:7437 LIFESCI
TI The influence of growth medium on serum sensitivity of Bacteroides species
AU Allan, E.; ***Poxton, I.R.****
CS Dep. Med. Microbiol., Univ. Edinburgh Med. Sch., Teviot Place, Edinburgh EH8 9AG, UK
SO J. MED. MICROBIOL., (1994) vol. 41, no. 1, pp. 45-50. ISSN: 0022-2615.
DT Journal
FS J
LA English
SL English
AB The susceptibility of 12 different Bacteroides strains (representing nine species) to the bactericidal effect of human serum complement was investigated. When grown in nutrient-rich proteose peptone-yeast extract medium, all 12 strains were, to varying degrees, sensitive to serum. However, when grown in Van Tassell and Wilkins's minimal medium, six of the 12 strains became markedly more serum resistant. Five of these six strains became totally resistant to serum when grown in heat-inactivated (56 degree C, 30 min) sheep serum. By Percoll discontinuous density centrifugation and light microscopy, the ratio of bacteria with large and small capsules was found to vary with the growth medium used. Lipopolysaccharide (LPS) was extracted with aqueous phenol after growth in the three media. Polyacrylamide gel electrophoresis (PAGE) and silver staining of the LPS showed some differences in LPS profiles in all strains tested. Therefore, variation of growth conditions results in alterations of both the expression of surface structures and, in some cases, sensitivity to serum. The biochemical basis for these changes requires further investigation.

L6 ANSWER 39 OF 57 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 18
AN 1993:478500 BIOSIS
DN PREV199396112100
TI A broadly cross-protective monoclonal antibody binding to Escherichia coli and Salmonella lipopolysaccharides.
AU Di Padova, Franco E. (1); Brade, Helmut; Barclay, G. Robin; ***Poxton,*** *** Ian R.*** ; Liehl, Ekke; Schuetze, Eberhard; Kocher, Hans P.; Ramsay, Graham; Schreier, Max H.; et al.
CS (1) Preclinical Res., Sandoz Pharma Ltd., CH-4002 Basel Switzerland
SO Infection and Immunity, (1993) Vol. 61, No. 9, pp. 3863-3872.
ISSN: 0019-9567.
DT Article
LA English
AB During the last decade, episodes of sepsis have increased and Escherichia coli has remained the most frequent clinical isolate. Lipopolysaccharides (LPS; endotoxin) are the major toxic and antigenic components of gram-negative bacteria and qualify as targets for therapeutic interventions. Molecules that neutralize the toxic effects of LPS are actively investigated. In this paper, we describe a murine monoclonal antibody (MAb; WN1 222-5), broadly cross-reactive and cross-protective for smooth (S)-form and rough (R)-form LPS. As shown in enzyme-linked immunosorbent assay and the passive hemolysis assay, WN1 222-5 binds to the five known E. coli core chemotypes, to Salmonella core, and to S-form LPS having these ewe structures. In immunoblots, it is shown to react with both the nonsubstituted core LPS and with LPS carrying O-side chains, indicating the exposure of the epitope in both S-form and R-form LPS. This MAb of the immunoglobulin G2a class is not lipid isolates is broad. WN1 222-5 binds to all E. coli clinical isolates tested so far (79 blood isolates, 80 urinary isolates, and 21 fecal isolates) and to some Citrobacter, Enterobacter, and Klebsiella isolates. This pattern of reactivity indicates that its binding epitope is widespread among members of the Enterobacteriaceae. WN1 222-5 exhibits biologically relevant activities. In vitro, it inhibits the Limulus amoebocyte lysate assay activity of S-form and R-form LPS in a dose-dependent manner and it neutralizes the LPS-induced release of clinically relevant monokines (interleukin 6 and tumor necrosis factor). In vivo, WN1 222-5 blocks endotoxin-induced pyrogenicity in rabbits and lethality in galactosamine-sensitized mice. The discovery of WN1 222-5 settles the long-lasting controversy over the existence of anti-core LPS MAbs with both cross-reactive and cross-protective activity, opening new possibilities for the immunotherapy of sepsis caused by gram-negative bacteria.

L6 ANSWER 40 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1993:122974 CAPLUS
DN 118:122974
TI Monoclonal and humanized antibodies against the lipopolysaccharide core antigen of gram-negative bacteria
IN Gram, Hermann; Di Padova, Franco; Barclay, George Robin; ***Poxton, Ian*** *** Raymond***
PA Sandoz Ltd., Switz.; Sandoz-Patent-G.m.b.H.
SO PCT Int. Appl., 83 pp.
CODEN: PIXXD2

DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9216624	A1	19921001	WO 1992-EP380	19920222
W: AU, BB, BG, BR, CA, CS, FI, HU, JP, KP, KR, LK, MG, MN, MW, NO, PL, RO, RU, SD, US				
RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, DE, DK, ES, FR, GA, GB, GN, GR, IT, LU, MC, ML, MR, NL, SE, SN, TD, TG				
CA 2105979	AA	19920914	CA 1992-2105979	19920222
AU 9212611	A1	19921021	AU 1992-12611	19920222
EP 576439	A1	19940105	EP 1992-904901	19920222
EP 576439	B1	19990506		
R: AT, CH, DE, DK, ES, FR, GB, IT, LI, NL, SE				
JP 06505867	T2	19940707	JP 1992-504918	19920222
AT 179753	E	19990515	AT 1992-904901	19920222
ES 2131526	T3	19990801	ES 1992-904901	19920222
US 5858728	A	19990112	US 1996-647144	19960509
PRAI GB 1991-5292		19910313		
WO 1992-EP380		19920222		
US 1993-119046		19930930		

AB Antibodies that recognize the lipopolysaccharide of gram-neg. bacteria and so are useful in the treatment of gram-neg. bacteremia are prepd. and humanized antibodies are prepd. from them. Hybridomas were prepd. by std. methods using spleen cells from mice immunized with killed gram-neg. bacteria. The cDNAs encoding the variable regions were cloned by PCR using amino acid sequence-derived primers and these were ligated to human const. region cDNAs to generate humanized antibody cDNAs. Expression of the cDNAs for 2 such antibodies in SP2/0 cells is demonstrated.

L6 ANSWER 41 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1993:120524 CAPLUS
DN 118:120524
TI Monoclonal antibodies as probes for detecting lipopolysaccharide expression on Escherichia coli from different growth conditions
AU Nelson, David; Bathgate, Andrew J.; ***Poxton, Ian R.***
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO J. Gen. Microbiol. (1991), 137(12), 2741-51
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal
LA English
AB Monoclonal antibody (mAb) probes were used to investigate the expression of lipopolysaccharide (LPS) on 4 E. coli strains grown under a variety of conditions in batch culture which mimicked some of the in vivo environmental conditions of an infected host. Techniques of Ag staining, immunoblotting, whole cell ELISA, and flow cytometry were all used to monitor the expression of LPS on the bacteria and the binding of the anti-LPS mAbs. Growth in heat-inactivated sheep serum and Mg-depleted conditions demonstrated increased expression of LPS core and subsequent increased binding of anti-core mAbs. Mg-depleted conditions also resulted in decreased prodn. of O-polysaccharide material. Fe-depleted bacteria showed only minor changes in LPS expression, although increased binding of anti-core mAbs was obsd. N-deficient/high-C conditions, chosen to promote

capsule prodn., resulted in increased expression of O-polysaccharide and decreased binding of anti-core mAbs.

L6 ANSWER 42 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1990:587729 CAPLUS
DN 113:187729
TI Characterization of Bacteroides from sheep periodontal disease by SDS-PAGE of outer membrane proteins
AU McCourtie, Jane; ***Poxton, Ian R.***
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO FEMS Microbiol. Lett. (1990), 71(1-2), 5-9
CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB Isolates of Bacteriodes species obtained from a longitudinal study of developing periodontal disease in sheep were analyzed by SDS-PAGE. Protein profiles of Sarkosyl-insol. outer membrane exts. were compared within groups of isolates which had already been defined by conventional biochem. techniques. Heterogeneity was exhibited within most groups. Isolates of B. gingivalis and B. asaccharolyticus, shown to be similar to human isolates by conventional biochem. tests, gave different protein profiles from the resp. type cultures. The sheep B. gingivalis-like isolates were, however, homogeneous, while the B. asaccharolyticus-like organisms could be divided into 3 subgruops. SDS-PAGE appears to be a useful tool for the examn. of bacterial flora and recognition of subgroups or subspecies.

L6 ANSWER 43 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1988:626363 CAPLUS
DN 109:226363
TI The cell wall proteins of Clostridium difficile
AU Sharp, Jacqueline; ***Poxton, Ian R.***
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO FEMS Microbiol. Lett. (1988), 55(1), 99-103
CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB The proteins which can be released by 6M urea treatment from the cell walls of C. difficile represent the major cell surface proteins. In the 5 strains examd., there are one to three of these major proteins. They appear to be strain-specific antigens, being detected in immunoblots only with homologous antiserum. A common cell-surface protein of Mr 73 kDa has been identified as a minor component of the urea ext.

L6 ANSWER 44 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1986:587237 CAPLUS
DN 105:187237
TI Immunochemistry of the surface carbohydrate antigens of Bacteroides fragilis and definition of a common antigen
AU ***Poxton, Ian R.*** ; Brown, Robert
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO J. Gen. Microbiol. (1986), 132(9), 2475-81
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal

LA English
AB The components extd. by aq. phenol from whole cells of B. fragilis were analyzed by SDS-PAGE and immunoblotting and shown to consist of a series of strain-specific, cross-reactive, and common antigens. Regularly-spaced ladder patterns on Ag-stained gels indicated that in most strains the lipopolysaccharide (LPS) was present as a predominantly smooth type, but with chain lengths of varying mol. mass, ranging within each particular strain from essentially rough forms to long chain-length smooth forms. The rough form of the LPS at the gel front possessed an antigen common to most of the strains investigated. Another antigen, which migrated behind the rough LPS on SDS gels, was common to all strains of the species. The smooth LPS forms and the other high mol. mass components were strain-specific antigens. Previously published methods are not capable of producing pure LPS or capsular polysaccharide for this organism.

L6 ANSWER 45 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1986:166541 CAPLUS
DN 104:166541
TI Analysis of the membrane lipocarbohydrate antigen of Clostridium difficile by polyacrylamide gel electrophoresis and immunoblotting
AU Sharp, Jacqueline; ***Poxton, Ian R.***
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO FEMS Microbiol. Lett. (1986), 34(1), 97-100
CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB The membrane lipocarbohydrate antigen (lipoteichoic acid analog) of C. difficile was purified by aq. phenol extn. and Sepharose 6B chromatog. After anal. by PAGE and immunoblotting, the antigen was shown to consist of a series of components of differing mol. wts. It appears as a regularly spaced ladder pattern similar to that shown for the lipopolysaccharide of many Gram-neg. bacteria.

L6 ANSWER 46 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1985:403330 CAPLUS
DN 103:3330
TI The association on SDS-polyacrylamide gels of lipopolysaccharide and outer membrane proteins of Pseudomonas aeruginosa as revealed by monoclonal antibodies and Western blotting
AU ***Poxton, Ian R.*** ; Bell, Graham T.; Barclay, G. Robin
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO FEMS Microbiol. Lett. (1985), 27(2), 247-51
CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB Monoclonal antibodies raised against single serotype components of a P. aeruginosa vaccine were shown to bind to the O antigen region of lipopolysaccharide (LPS). Outer membrane (OM) proteins, prepd. by detergent treatment of envelope fractions and by EDTA/sonication treatment of whole cells, were sepd. on SDS-polyacrylamide gel electrophoresis, electrophoretically transferred to nitrocellulose membrane, and reacted with LPS-specific monoclonal antibodies. The patterns produced revealed that many of the protein bands were in fact protein-LPS complexes.

L6 ANSWER 47 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1986:4370 CAPLUS
DN 104:4370
TI An immunochemical method for fingerprinting Clostridium difficile
AU Sharp, Jacqueline; ***Poxton, Ian R.***
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO J. Immunol. Methods (1985), 83(2), 241-8
CODEN: JIMMBG; ISSN: 0022-1759
DT Journal
LA English
AB The use of SDS-polyacrylamide gel electrophoresis in assocn. with electrophoretic transfer of proteins to nitrocellulose and subsequent probing with antisera appears useful as a method for peptide fingerprinting C. difficile. Thorough testing of the stability of the antigenic nature of isolates of the organism during subculture and antigen prepn. has shown it to be remarkably stable both in vitro and in vivo. Minor differences in the method of antigen extn. do not markedly alter the immunoblot patterns produced. It has also been demonstrated that an individual may harbor more than 1 strain of the organism at any 1 time. Results show the possible usefulness of this technique in studying the epidemiol. of diarrheal disease known to be assocd. with C. difficile. It is suggested that for any serious study several colonies should be subcultured from the primary isolation plate.

L6 ANSWER 48 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1984:436997 CAPLUS
DN 101:36997
TI Demonstration of the common antigens of Clostridium botulinum, C. sporogenes and C. novyi by an enzyme-linked immunosorbent assay and electroblot transfer
AU ***Poxton, Ian R.***
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO J. Gen. Microbiol. (1984), 130(4), 975-81
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal
LA English
AB EDTA exts. were prepd. from whole cells of 16 strains of C. botulinum (types A-E), 6 strains of C. novyi (types A-D), and 3 strains of C. sporogenes. They were reacted in an ELISA with antisera raised against whole, UV-killed cells of C. sporogenes and C. novyi type A. Results showed significant cross-reactions between C. sporogenes antiserum and the C. botulinum type A (3 out of 4 strains), proteolytic type B (all strains), and 1 type E strain, and between C. novyi type A antiserum and C. botulinum types C and D. All the C. sporogenes and C. novyi strains reacted with their homologous antiserum; these 2 species showed no cross-reactions. All the reactions were investigated further by running the EDTA exts. on SDS-polyacrylamide gels. The sepd. mols. were electrophoretically transferred to nitrocellulose membranes, reacted with antiserum, and complexes were visualized with horseradish peroxidase conjugate reagents. Only those exts. that reacted significantly in the ELISA gave a pattern of cross-reactive antigen bands, and the no. of bands and intensity of stain closely paralleled the strength of the ELISA reaction.

L6 ANSWER 49 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1984:31782 CAPLUS
DN 100:31782
TI Analysis of lipopolysaccharides of Bacteroides fragilis by sodium dodecyl sulfate-polyacrylamide gel electrophoresis and electroblot transfer
AU Cousland, Gary; ***Poxton, Ian R.***
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO FEMS Microbiol. Lett. (1983), 20(3), 461-5
CODEN: FMLED7; ISSN: 0378-1097
DT Journal
LA English
AB Lipopolysaccharides (LPS) from 3 strains of B. fragilis were run on SDS-polyacrylamide gels and stained with Ag. Each LPS produced a similar pattern, consisting of a series of regularly spaced discrete bands which decreased in intensity as they increased in mol. wt. (Mr) value. Electroblot transfer from duplicate SDS gels onto nitrocellulose membrane were reacted with antisera raised to whole cells of 2 of the strains and antigens were visualized with horseradish peroxidase-anti-rabbit-IgG conjugate and color reagent. Results revealed that the 2 lowest Mr bands of the LPS prepn. (rough LPS) represented common antigens.

L6 ANSWER 50 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1982:525453 CAPLUS
DN 97:125453
TI Immunochemistry of the cell-surface carbohydrate antigens of Clostridium difficile
AU ***Poxton, Ian R.*** ; Cartmill, T. D. Ivor
CS Dep. Bacteriol., Univ. Edinburgh Med. Sch., Edinburgh, EH8 9AG, UK
SO J. Gen. Microbiol. (1982), 128(6), 1365-70
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal
LA English
AB Two carbohydrate cell-surface antigens were extd. from C. difficile. One was extd. from pure cell walls by NaOH and contained glucose, mannose, galactosamine, and phosphate in the approx. molar proportions of 2:0.65:1:0.63. The other antigen was extd. with phenol from the disrupted contents of whole cells and purified by chromatog. on Sepharose 6B and an immunoadsorbent column; it contained glucose, glucosamine, phosphate, and fatty acid in the approx. molar proportions of 2:1:1.6:0.04. Both antigens showed partial immunol. identity and both cross-reacted with C. sordellii antiserum. These antigens are analogs of the wall and membrane teichoic acids of other Gram-pos. bacteria.

L6 ANSWER 51 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1981:544793 CAPLUS
DN 95:144793
TI Detection of Clostridium difficile toxin by counterimmunoelectrophoresis: a note of caution
AU ***Poxton, Ian R.*** ; Byrne, Marie D.
CS Med. Sch., Univ. Edinburgh, Edinburgh, EH8 9AG, Scot.
SO J. Clin. Microbiol. (1981), 14(3), 349
CODEN: JCMIDW; ISSN: 0095-1137
DT Journal
LA English

AB Recent methods for detection of C. difficile toxin by counterimmunoelectrophoresis might lead to errors. False-positives may be attributable to sol. cell surface antigens reacting with impure antitoxin.

L6 ANSWER 52 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1982:118560 CAPLUS
DN 96:118560
TI The cell-surface antigens of Bacteroides vulgatus
AU ***Poxton, Ian R.*** ; Ip, Madeleine K. Y.
CS Dep. Bacteriol., Univ. Edinburgh, Edinburgh, EH8 9AG, UK
SO J. Gen. Microbiol. (1981), 126(1), 103-9
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal
LA English
AB The cell surface of B. vulgatus was examd. by electron microscopy. The outer membrane complex was removed by EDTA and mild sonication and the antigens of this complex were characterized by enzyme-linked immunosorbent assay and crossed immunoelectrophoresis. The species-specific antigen was identified and was shown to be the major outer membrane protein with a mol. wt. of 100,000.

L6 ANSWER 53 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1981:513137 CAPLUS
DN 95:113137
TI Immunological analysis of the EDTA-soluble antigens of Clostridium difficile and related species
AU ***Poxton, Ian R.*** ; Byrne, Marie D.
CS Dep. Bacteriol., Univ. Edinburgh Med. Sch., Edinburgh, EH8 9AG, Scot.
SO J. Gen. Microbiol. (1981), 122(1), 41-6
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal
LA English
AB Enzyme-linked immunosorbent assay studies of the EDTA-extd. antigens from 32 strains representing 10 species of Clostridium showed marked crossreactions between C. difficile, C. sordellii, and C. bifermentans. The crossreactive antigen, visualized by crossed immunoelectrophoresis, was carbohydrate.

L6 ANSWER 54 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1980:2900 CAPLUS
DN 92:2900
TI Sodium dodecyl sulfate-polyacrylamide gel electrophoresis of cell-surface proteins as an aid to the identification of the Bacteroides fragilis group
AU ***Poxton, Ian R.*** ; Brown, Robert
CS Bacteriol. Dep., Univ. Edinburgh Med. Sch., Edinburgh, EH8 9AG, Scot.
SO J. Gen. Microbiol. (1979), 112(2), 211-17
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal
LA English
AB Na dodecyl sulfate-polyacrylamide gel electrophoresis on slab gels of the outer membrane complexes released by EDTA treatment from 8 species of the B. fragilis group showed marked intraspecies similarities of the surface protein patterns, whereas fewer similarities were obsd. in patterns produced by strains belonging to different species. An unknown organism

could be identified to species level using this technique combined with selected biochem. tests.

L6 ANSWER 55 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1979:199176 CAPLUS
DN 90:199176
TI The structure of C-polysaccharide from the walls of Streptococcus pneumoniae
AU ***Poxton, Ian R.*** ; Tarelli, Edward; Baddiley, James
CS Microbiol. Chem. Res. Lab., Univ. Newcastle upon Tyne, Newcastle upon Tyne, Engl.
SO Biochem. J. (1978), 175(3), 1033-42
CODEN: BIJOAK; ISSN: 0306-3275
DT Journal
LA English
AB Structural features of C-polysaccharide prepd. from the cell walls of S. pneumoniae were established by chem. and spectral means. The order of substituents, the location of positions of substitution, and the configuration of anomeric centers in the repeating unit of the polymer are proposed.

L6 ANSWER 56 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1979:416403 CAPLUS
DN 91:16403
TI The uptake of choline by Streptococcus pneumoniae
AU Thomas, A. Mavis; Lambert, Peter A.; ***Poxton, Ian R.***
CS Microbiol. Chem. Res. Lab., Univ. Newcastle upon Tyne, Newcastle upon Tyne, Engl.
SO J. Gen. Microbiol. (1978), 109(2), 313-17
CODEN: JGMIAN; ISSN: 0022-1287
DT Journal
LA English
AB The very efficient uptake of choline-3H chloride by S. pneumoniae ([S]0.5 3.2 .mu.M, where [SS]0.5 is the solute concn. giving 50% the max. rate of uptake) was inhibited by 100, 64, and 12% by iodoacetate (1 mM), dinitrophenol (1 mM), and oligomycin (0.25 mM), resp., but was not affected by structural analogs of choline (5 .mu.M). Ethanolamine[3H]-HCl was transported in the absence of choline, but with a reduced affinity ([SS]0.5 71.4 .mu.M). The same constitutive system is probably used by both choline and ethanolamine; it may require ATP and involve choline kinase.

L6 ANSWER 57 OF 57 CAPLUS COPYRIGHT 2001 ACS
AN 1977:530187 CAPLUS
DN 87:130187
TI The biosynthesis of a choline nucleotide by a cell-free extract from Streptococcus pneumoniae
AU ***Poxton, Ian R.*** ; Leak, David J.
CS Microbiol. Chem. Res. Lab., Univ. Newcastle upon Tyne, Newcastle upon Tyne, Engl.
SO J. Gen. Microbiol. (1977), 100(1), 23-9
CODEN: JGMIAN
DT Journal
LA English

AB Cell-free exts. of S. pneumoniae converted choline to cytidine diphosphocholine via choline phosphate. Choline kinase (EC 2.7.1.32) of S. pneumoniae had a pH optimum of 7.3-7.4 and was stimulated by Mg2+. The Km values of choline kinase for ATP and choline were 1 and 0.19mM, resp., with corresponding Vmax values of 3 and 0.5 nmol/min/mg protein. CDP-choline pyrophosphorylase of S. pneumoniae was specific for CTP and had a requirement for Mg2+ with an optimum at 7mM.

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E2 1 MCINTOSH THOMAS HENRY/AU
E3 83 --> MCINTOSH THOMAS J/AU
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E9 3 MCINTOSH TINA C/AU
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E11 2 MCINTOSH TRACEY K/AU
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L8 ANSWER 1 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2001:232954 BIOSIS
DN PREV200100232954
TI Influence of lipid composition on physical properties and PEG-mediated fusion of curved and uncurved model membrane vesicles: "Nature's own" fusogenic lipid bilayer.
AU Haque, Md. Emdadul; ***McIntosh, Thomas J.*** ; Lentz, Barry R. (1)
CS (1) Department of Biochemistry and Program in Molecular/Cell Biophysics, University of North Carolina, Chapel Hill, NC, 27599-7260: uncbrl@med.unc.edu USA
SO Biochemistry, (April 10, 2001) Vol. 40, No. 14, pp. 4340-4348. print. ISSN: 0006-2960.
DT Article
LA English
SL English
AB Poly(ethylene glycol) (PEG)-mediated fusion of phosphatidylcholine model membranes has been shown to mimic the protein-mediated biomembrane process (Lee, J., and Lentz, B. R. (1998) Proc. Natl. Acad. Sci. U.S.A. 95, 9274-9279). Unlike the simple model membranes used in this earlier study, the lipid composition of fusogenic biomembranes is quite complex. The

purpose of this paper was to examine PEG-mediated fusion of highly curved (SUV) and largely uncurved (LUV) membrane vesicles composed of different lipids in order to identify lipid compositions that produce highly fusogenic membranes. Starting with liposomes composed of five lipids with different physical properties, dioleoylphosphatidylcholine (DOPC), dioleoylphosphatidylethanolamine (DOPE), dioleoylphosphatidylserine (DOPS), bovine brain sphingomyelin (SM), and cholesterol (CH), we systematically varied the composition and tested for the extent of PEG-mediated fusion after 5 min of treatment. We found that a vesicle system composed of four lipids, DOPC/DOPE/SM/CH, fused optimally at a 35/30/15/20 molar ratio. Each lipid seemed to play a part in optimizing the membrane for fusion. PE disrupted outer leaflet packing as demonstrated with TMA-DPH lifetime, C6-NBD-PC partitioning, and DPH anisotropy measurements, and thus significantly enhanced fusion and rupture, without significantly altering interbilayer approach (X-ray diffraction). An optimal ratio of PC/PE (35/30) produced a balance between fusion and rupture. CH and SM, when present at an optimal ratio of 3/4 in vesicles containing the optimal PC/PE ratio, reduced rupture without significantly reducing fusion. This optimal CH/SM ratio also enhanced outer leaflet packing, suggesting that fusion is dependent not only on outer leaflet packing but also on the properties of the inner leaflet. Addition of CH without SM enhanced rupture relative to fusion, while SM alone reduced both rupture and fusion. The optimal lipid composition is very close to the natural synaptic vesicle composition, suggesting that the synaptic vesicle composition is optimized with respect to fusogenicity.

L8 ANSWER 2 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:157255 BIOSIS
DN PREV200100157255
TI The effect of ethanol on the phase transition temperature and the phase structure of monounsaturated phosphatidylcholines.
AU ***McIntosh, Thomas J.*** ; Lin, Hainan; Li, Shusen; Huang, Ching-hsien (1)
CS (1) Department of Biochemistry and Molecular Genetics, University of Virginia School of Medicine, Charlottesville, VA, 22908: ch9t@virginia.edu USA
SO Biochimica et Biophysica Acta, (9 February) Vol. 1510, No. 1-2, pp. 219-230. print.
ISSN: 0006-3002.
DT Article
LA English
SL English
AB Previous studies from our laboratories have delineated the relationship between the acyl chain asymmetry of mixed-chain phosphatidylcholines, C(X):C(Y)PC, and the effect of ethanol concentration, (EtOH), on the main phase transition temperature, Tm, and the phase structure of the lipid bilayer composed of C(X):C(Y)PC using differential scanning calorimetry and X-ray diffraction techniques (Huang and McIntosh, Biophys. J. 72 (1997) 2702-2709). In the present work, we have extended these studies to characterize the effect of (EtOH) on the Tm and the phase structure of the lipid bilayer composed of sn-1 saturated/sn-2 monounsaturated phosphatidylcholines with various positions of the cis double bond. Specifically, five positional isomers of 1-eicosanoyl-2-eicosenoyl-sn-

glycero-3-phosphocholines, C(20):C(20:1DELTAn)PC with n = 5, 8, 11, 13 and 17, were synthesized and studied. For C(20):C(20:1DELTAn)PC with n = 5 and 8, results from the calorimetric experiments showed that in response to various concentrations of ethanol, the change in Tm of the lipid bilayer composed of monounsaturated lipids was characterized by a sigmoidal or biphasic profile in the plot of Tm versus (EtOH). In contrast, a continuous depression of the Tm by ethanol was observed calorimetrically for C(20):C(20:1DELTAn)PC with n gtoreq 11. The X-ray diffraction experiments further demonstrated that C(20):C(20:1DELTA5)PC and C(20):C(20:1DELTA8)PC can undergo the ethanol-induced gel-to-fully interdigitated phase transition at T < Tm. Such a transition, however, was not observed for C(20):C(20:1DELTA13)PC even at a very high ethanol concentration of 100 mg/ml. These distinct different effects of (EtOH) on the phase transition temperature and the phase structure can be attributed to various positions of the cis double bond in these monounsaturated phosphatidylcholines. And the different effects of ethanol can, in fact, be explained based on the molecular structures of these monounsaturated lipids packed in the gel-state bilayer as generated by molecular mechanics simulations. To the best of our knowledge, this is the first time that the ethanol-induced fully interdigitated bilayers are observed at T < Tm for unsaturated phospholipids with well defined double bond positions in their sn-2 acyl chains.

L8 ANSWER 3 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 2001:199307 CAPLUS
TI Physical properties of novel carbohydrate based phospholipid bilayers
AU Hird, Geoffrey S.; Lee, Stephen; ***McIntosh, Thomas J.*** ; Grinstaff, Mark W.
CS Department of Chemistry, Duke University, Durham, NC, 27708-0348, USA
SO Abstr. Pap. - Am. Chem. Soc. (2001), 221st, COLL-057
CODEN: ACSRAL; ISSN: 0065-7727
PB American Chemical Society
DT Journal; Meeting Abstract
LA English
AB A novel phospholipid based upon a carbohydrate backbone, methyl-2,3-di-O-myristoyl-beta-D-ribo-5-phosphocholine (DMRPC), has been synthesized and characterized. This mol. self-assembles in aq. soln. to form lipid bilayers which have been examd. using Modulated Differential Scanning Calorimetry (MDSC), Optical Microscopy, and X-ray Diffraction. Phys. studies of the bilayer structures, which have been named -carbohydrosomes', revealed properties significantly different than those obsd. with conventional glycerol based phospholipids. In particular, an elevated gel-liq. crystal phase transition temp. was obsd. and a more stable Lc phase exists below the phase transition temp. In an effort to better understand these results and to provide further phys. properties of the bilayer, the mixing behavior of DMPC with DMRPC was studied using MDSC. The orientation of the novel phospholipid in the bilayer membrane was also investigated by 1H-NMR line broadening expts. on the supramol. structures in water.

L8 ANSWER 4 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:139534 BIOSIS
DN PREV200100139534
TI Structure of detergent-insoluble lipid domains.

AU ***McIntosh, Thomas J. (1)*** ; Vidal, A. (1); Gandhavadi, M. (1); Simon, S. A. (1)
CS (1) Depts. of Cell Biology and Neurobiology, Duke University Medical Center, Durham, NC USA
SO Biophysical Journal, (January, 2001) Vol. 80, No. 1 Part 2, pp. 24a. print.
Meeting Info.: 45th Annual Meeting of the Biophysical Society Boston, Massachusetts, USA February 17-21, 2001 Biophysical Society . ISSN: 0006-3495.
DT Conference
LA English
SL English

L8 ANSWER 5 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
AN 2000:485034 BIOSIS
DN PREV200000485034
TI The lipopolysaccharide barrier: Correlation of antibiotic susceptibility with antibiotic permeability and fluorescent probe binding kinetics.
AU Snyder, D. Scott; ***McIntosh, Thomas J. (1)***
CS (1) Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710 USA
SO Biochemistry, (September 26, 2000) Vol. 39, No. 38, pp. 11777-11787. print.
ISSN: 0006-2960.
DT Article
LA English
SL English
AB Lipopolysaccharide (LPS), the primary lipid on the surface of Gram-negative bacteria, is thought to act as a permeability barrier, making the outer membrane relatively impermeable to hydrophobic antibiotics, detergents, and host proteins. Mutations in the LPS biosynthetic apparatus increase bacterial susceptibility to such agents. To determine how this increased susceptibility is mediated, we have correlated antibiotic susceptibilities of rough (antibiotic resistant) and deep rough (antibiotic susceptible) bacterial strains with antibiotic permeabilities and fluorescent probe binding kinetics for bilayers composed of LPS purified from the same strains. Bilayer permeabilities of two hydrophobic beta-lactam antibiotics were measured by encapsulating the appropriate beta-lactamases in large unilamellar vesicles. In the presence of MgCl2, permeabilities of LPS bilayers from rough and deep rough bacteria were similar and significantly lower than those of bacterial phospholipids (BPL). Addition of BPL to the LPS bilayers increased their antibiotic permeability to approximately the level of the BPL bilayers. Binding rates of the fluorescent probe bis-aminonaphthylsulfonic acid (BANS) were 2 orders of magnitude slower for both rough and deep rough LPS bilayers compared to that of bilayers composed of BPL or mixtures of LPS and BPL. On the basis of these results and the observation that deep rough bacteria have higher levels of phospholipid on their surface than do rough bacteria (Kamio, Y., and Nikaido, H. (1976) Biochemistry 15, 2561-2569), we argue that the high susceptibility of deep rough bacteria is due to the presence of phospholipids on their surface. Experiments with phospholipid bilayers showed that the addition of PEG-lipids (containing covalently attached hydrophilic polymers) had little effect on permeability and binding rates, whereas the addition of cholesterol reduced permeability

and slowed binding to levels approaching those of LPS. Therefore, we argue that the barrier provided by LPS is primarily due to its tight hydrocarbon chain packing (Snyder et al., (1999) Biochemistry 38, 10758-10767) rather than to its polysaccharide headgroup.

L8 ANSWER 6 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 2000:537863 CAPLUS
DN 133:277823
TI Supramolecular Structures of Novel Carbohydrate-Based Phospholipids
AU Hird, Geoffrey S.; ***McIntosh, Thomas J.*** ; Grinstaff, Mark W.
CS Department of Chemistry Paul M. Gross Chemical Laboratory, Duke University, Durham, NC, 27708, USA
SO J. Am. Chem. Soc. (2000), 122(33), 8097-8098
CODEN: JACSAT; ISSN: 0002-7863
PB American Chemical Society
DT Journal
LA English
OS CASREACT 133:277823
AB The authors report here the synthesis and phys. characterization of DLRPC and formation of supramol. structures with DLPC.
RE.CNT 30
RE
(1) Ahmad, T; Chem Phys Lipids 1990, V55, P231 CAPLUS
(2) Bangham, A; J Mol Biol 1964, V8, P660 CAPLUS
(3) Batrakov, S; Biophys Acta 1997, V1347, P127 CAPLUS
(4) Bhattacharya, S; Chem Commun 1997, P2287 CAPLUS
(5) Blaurock, A; Biochemsitry 1986, V25, P299 CAPLUS
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L8 ANSWER 7 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
AN 2000:534435 BIOSIS
DN PREV200000534435
TI Preparation and preclinical evaluation of a novel liposomal complete-core lipopolysaccharide vaccine.
AU Bennett-Guerrero, Elliott (1); ***McIntosh, Thomas J.*** ; Barclay, G. Robin; Snyder, D. Scott; Gibbs, Richard J.; Mythen, Michael G.; Poxton, Ian R.
CS (1) Department of Anesthesiology, Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York, NY, 10032-3784 USA
SO Infection and Immunity, (November, 2000) Vol. 68, No. 11, pp. 6202-6208. print.
ISSN: 0019-9567.
DT Article
LA English
SL English
AB Our objective is to develop a prophylactic vaccine strategy that can be evaluated for surgical and other high-risk hospitalized patients. In this paper, we describe the preparation and preclinical evaluation of a liposomal complete-core lipopolysaccharide (LPS) vaccine that is nontoxic and broadly antigenic. Complete-core (Ra-chemotype) LPSs were isolated from four gram-negative bacterial strains (Escherichia coli K-12, E. coli R1, Pseudomonas aeruginosa PAC608, and Bacteroides fragilis), mixed together to form a cocktail of complete-core LPSs, and then incorporated into multilamellar liposomes consisting of dimyristoyl phosphatidyl

choline, dimyristoyl phosphatidylglycerol, and cholesterol in a 4:1:4 molar ratio. The endotoxic activities of these LPS-containing liposomes were less than 0.1% of the endotoxicities of the original free LPSs as measured by the Limulus amoebocyte lysate assay. In vivo administration of liposomal complete-core LPS mixed with Al(OH)3 to rabbits resulted in no pyrogenicity or overt toxicity over a 7-day period. In immunoblots, sera from rabbits following active immunization elicited cross-reactive antibodies to a large panel of rough and smooth LPSs from numerous clinically relevant gram-negative bacteria, including E. coli (serotypes O1, O4, O6, O8, O12, O15, O18, O75, O86, O157, and O111), P. aeruginosa (Fisher-Devlin serotypes 1, 2, and 3, which correspond to International Antigenic Typing Scheme types 6, 11, and 2, respectively), Klebsiella pneumoniae (serotypes O1, O2ab, and O3), B. fragilis, and Bacteroides vulgatus. Active immunization of mice with liposomal complete-core LPS provided protection against a lethal challenge with E. coli O18 LPS. The vaccine tested was nontoxic, nonpyrogenic, and immunogenic against a wide variety of pathogens found in clinical settings.

L8 ANSWER 8 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
AN 2001:60136 BIOSIS
DN PREV200100060136
TI Electrostatic control of phospholipid polymorphism.
AU Tarahovsky, Yury S.; Arsenault, A. Larry; MacDonald, Robert C. (1); ***McIntosh, Thomas J.*** ; Epand, Richard M.
CS (1) Department of Biochemistry, Molecular Biology, and Cell Biology, Northwestern University, 2153 Campus Drive, Evanston, IL, 60208-3500: macd@northwestern.edu USA
SO Biophysical Journal, (December, 2000) Vol. 79, No. 6, pp. 3193-3200. print.
ISSN: 0006-3495.
DT Article
LA English
SL English
AB A regular progression of polymorphic phase behavior was observed for mixtures of the anionic phospholipid, cardiolipin, and the cationic phospholipid derivative, 1,2-dioleoyl-sn-glycero-3-ethylphosphocholine. As revealed by freeze-fracture electron microscopy and small-angle x-ray diffraction, whereas the two lipids separately assume only lamellar phases, their mixtures exhibit a symmetrical (depending on charge ratio and not polarity) sequence of nonlamellar phases The inverted hexagonal phase, H11, formed from equimolar mixtures of the two lipids, i.e., at net charge neutrality (charge ratio (CR(+/-)) = 1:1). When one type of lipid was in significant excess (CR(+/-) = 2:1 or CR(+/-) = 1:2), a bicontinuous cubic structure was observed. These cubic phases were very similar to those sometimes present in cellular organelles that contain cardiolipin. Increasing the excess of cationic or anionic charge to CR(+/-) = 4:1 or CR(+/-) = 1:4 led to the appearance of membrane bilayers with numerous interlamellar contacts, i.e., sponge structures. It is evident that interactions between cationic and anionic moieties can influence the packing of polar heads and hence control polymorphic phase transitions. The facile isothermal, polymorphic interconversion of these lipids may have important biological and technical implications.

L8 ANSWER 9 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5

AN 2000:417380 BIOSIS
DN PREV200000417380
TI Short-range interactions between lipid bilayers measured by X-ray diffraction.
AU ***McIntosh, Thomas J. (1)***
CS (1) Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710 USA
SO Current Opinion in Structural Biology, (August, 2000) Vol. 10, No. 4, pp. 481-485. print.
ISSN: 0959-440X.
DT Article
LA English
SL English

L8 ANSWER 10 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:178239 BIOSIS
DN PREV200000178239
TI Cationic triesters of phosphotidylcholine: The effect of varying alkyl chain length on their physical properties and transfection activity.
AU Rakhmanova, Vera A. (1); ***McIntosh, Thomas J.*** ; MacDonald, Robert C. (1)
CS (1) Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Evanston, IL, 60208 USA
SO Biophysical Journal, (Jan., 2000) Vol. 78, No. 1 Part 2, pp. 329A. Meeting Info.: 44th Annual Meeting of the Biophysical Society. New Orleans, Louisiana, USA February 12-16, 2000
ISSN: 0006-3495.
DT Conference
LA English
SL English

L8 ANSWER 11 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AN 2000:368978 BIOSIS
DN PREV200000368978
TI O-alkyl dioleoylphosphatidylcholinium compounds: The effect of varying alkyl chain length on their physical properties and in vitro DNA transfection activity.
AU Rosenzweig, Howard S.; Rakhmanova, Vera A.; ***McIntosh, Thomas J.*** ; MacDonald, Robert C. (1)
CS (1) Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Evanston, IL, 60208 USA
SO Bioconjugate Chemistry, (May June, 2000) Vol. 11, No. 3, pp. 306-313. print.
ISSN: 1043-1802.
DT Article
LA English
SL English
AB 1,2-Dioleoyl-sn-3-ethylphosphocholine (EDOPC) has been previously shown be a highly effective DNA transfection reagent in vitro. To assess the effect of alkyl chain length on transfection efficiency, the O-methyl, O-propyl, O-hexyl, O-octadecyl derivatives have been prepared from dioleoylphosphatidylcholine using the corresponding alkyl trifluoromethylsulfonate. The methyl, ethyl, and propyl derivatives formed liposomes which were very large and unilamellar. The ethyl and propyl

derivatives were equally efficient at mediating transfection (even in the presence of serum) of BHK cells, but the chemically labile methyl derivative was a much weaker transfection agent. The O-decyl and O-octadecyl compounds, which assume the inverted hexagonal phase in excess water (as determined by X-ray diffraction), were almost inactive after manual agitation in both water and in saline; however, after sonication, these compounds exhibited good transfection activity. The O-hexyl derivative displayed novel behavior, assuming the lamellar phase at low and a cubic phase at high ionic strength. All compounds, whether lamellar or not, formed lamellar structures when complexed with DNA. In water, where the hexyl compound dispersed well, sonication diminished transfection activity, whereas at physiological ionic strength, which led to poor manual dispersion, sonication was essential for good transfection. These results emphasize the importance of optimal dispersion of a cationic lipid: too little, and interaction with DNA is handicapped, too much, and the resultant particle transfects poorly. Lipid dispersibility is thus an important variable in assessing lipid transfection agents, and caution is advised in attributing too much significance to chemical structure until interaction with DNA has been optimized.

L8 ANSWER 12 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
AN 2000:226469 BIOSIS
DN PREV200000226469
TI Effects of dioleoylphosphatidylethanolamine on the activity and structure of O-alkyl phosphatidylcholine-DNA transfection complexes.
AU Rakhmanova, Vera A. (1); ***McIntosh, Thomas J.*** ; MacDonald, Robert C. (1)
CS (1) Department of Biochemistry, Molecular Biology and Cell Biology, Northwestern University, Evanston, IL, 60208 USA
SO Cellular & Molecular Biology Letters, (2000) Vol. 5, No. 1, pp. 51-65. ISSN: 1425-8153.
DT Article
LA English
SL English
AB O-Alkyl derivatives of dioleoylphosphatidylcholine (DOPC) have been previously described as effective DNA transfection reagents. This communication reports the effects of the neutral helper lipid dioleoylphosphatidylethanolamine (DOPE) on the efficiency of transfection of BHK cells mediated by the O-ethyl-, O-hexyl-, and O-octadecyl- DOPC derivatives, compounds that by themselves are known to exhibit lyotropic phase preferences of lamellar, lamellar or cubic (depending on conditions) and inverse hexagonal, respectively. The effect of DOPE on transfection efficiency was found to be inhibition of the ethyl compound, stimulation or inhibition (depending on amount of DOPE) of the hexyl compound and stimulation in the case of the octadecyl compound, i.e., DOPE had a beneficial effect on the lipids that formed non-lamellar phases. X-ray diffraction was used to determine the lyotropic phase of the lipid-DOPE mixtures and of the lipid-DNA complex. DNA-lipid complexes tended to be lamellar unless the lipids had a very strong tendency toward the hexagonal phase, in which case the DNA complex was also hexagonal. Thus, a mixture of equal amounts of DOPE and hexyl-DOPC formed a lamellar complex with DNA, although the lipids on their own assumed the hexagonal phase. Octadecyl-DOPC formed a hexagonal phase with DOPE and the 1:1 DOPE mixture formed a hexagonal phase DNA complex; however, if smaller amounts of DOPE

were included, the complex had a lamellar structure, in contrast to the hexagonal phase of the lipids by themselves. For these cationic phospholipids, there was not necessarily a benefit to transfection of generating a hexagonal phase lipid-DNA complex.

L8 ANSWER 13 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 8
AN 1999:444105 BIOSIS
DN PREV199900444105
TI Lipopolysaccharide bilayer structure: Effect of chemotype, core mutations, divalent cations, and temperature.
AU Snyder, Scott; Kim, Dennis; ***McIntosh, Thomas J. (1)***
CS (1) Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710 USA
SO Biochemistry, (Aug. 17, 1999) Vol. 38, No. 33, pp. 10758-10767. ISSN: 0006-2960.
DT Article
LA English
SL English
AB Lipopolysaccharide (LPS), the primary lipid on the surface of Gram-negative bacteria, is thought to act as a protective and permeability barrier. X-ray diffraction analysis of osmotically stressed LPS multilayers was used to determine the structure and interactive properties of LPSs from strains containing the minimum number of sugars necessary for bacterial survival (Re chemotype) to the maximum number of sugars found in rough bacteria (Ra chemotype). At 20 degreeC in the absence of divalent cations, LPS suspensions gave a sharp wide-angle reflection at 4.23 ANG and a broad low-angle band centered at 50-68 ANG depending on the chemotype, indicating the presence of gel phase bilayers separated by large fluid spaces. As osmotic pressure was applied, the apposing bilayers were squeezed together and lamellar diffraction at 6 ANG resolution was obtained. At low applied pressures (< 106 dyn/cm2), the total repulsive pressure between bilayers could be explained by electrostatic double layer theory. At higher applied pressures, there was a sharp upward break in each pressure-distance relation, indicating the presence of a hydrophilic steric barrier whose range depended strongly on the LPS chemotype. The positions of these upward breaks, along with electron density profiles, showed that the sugar core width systematically increased from 10 ANG for the Re chemotype to 27 ANG for the Ra chemotype. In excess buffer, the addition of divalent cations brought the bilayers into steric contact. Electron density profiles were used to determine the locations of cation binding sites and polar substituents on the LPS oligosaccharide core. The area per hydrocarbon chain was approximately 26 ANG2 in liquid-crystalline LPS bilayers, an indication of an acyl chain packing that is much tighter than that found in bilayers composed of typical membrane lipids. This unusually tight packing could be a critical factor in the permeability barrier provided by LPS.

L8 ANSWER 14 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 9
AN 2000:26237 BIOSIS
DN PREV200000026237
TI Physical and biological properties of cationic triesters of phosphatidylcholine.
AU MacDonald, Robert C. (1); Ashley, Gary W.; Shida, Miho M.; Rakhmanova, Vera A.; Tarahovsky, Yury S.; Pantazatos, Dennis P.; Kennedy, Michael T.;

Pozharski, Edvin V.; Baker, Kent A.; Jones, Ramoun D.; Rosenzweig, Howard S.; Choi, Kenneth L.; Qiu, Ruozi; ***McIntosh, Thomas J.***

CS (1) Department of Biochemistry, Molecular Biology, and Cell Biology, Northwestern University, Evanston, IL, 60201-3500 USA

SO Biophysical Journal, (Nov., 1999) Vol. 77, No. 5, pp. 2612-2629. ISSN: 0006-3495.

DT Article

LA English

SL English

AB The properties of a new class of phospholipids, alkyl phosphocholine triesters, are described. These compounds were prepared from phosphatidylcholines through substitution of the phosphate oxygen by reaction with alkyl trifluoromethylsulfonates. Their unusual behavior is ascribed to their net positive charge and absence of intermolecular hydrogen bonding. The O-ethyl, unsaturated derivatives hydrated to generate large, unilamellar liposomes. The phase transition temperature of the saturated derivatives is very similar to that of the precursor phosphatidylcholine and quite insensitive to ionic strength. The dissociation of single molecules from bilayers is unusually facile, as revealed by the surface activity of aqueous liposome dispersions. Vesicles of cationic phospholipids fused with vesicles of anionic lipids. Liquid crystalline cationic phospholipids such as 1,2-dioleoyl-sn-glycero-3-ethylphosphocholine triflate formed normal lipid bilayers in aqueous phases that interacted with short, linear DNA and supercoiled plasmid DNA to form a sandwich-structured complex in which bilayers were separated by strands of DNA. DNA in a 1:1 (mol) complex with cationic lipid was shielded from the aqueous phase, but was released by neutralizing the cationic charge with anionic lipid. DNA-lipid complexes transfected DNA into cells very effectively. Transfection efficiency depended upon the form of the lipid dispersion used to generate DNA-lipid complexes; in the case of the O-ethyl derivative described here, large vesicle preparations in the liquid crystalline phase were most effective.

L8 ANSWER 15 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 10

AN 1999:227639 BIOSIS

DN PREV199900227639

TI Membrane fusion promoters and inhibitors have contrasting effects on lipid bilayer structure and undulations.

AU ***McIntosh, Thomas J. (1)*** ; Kulkarni, Ketan G.; Simon, Sidney A.

CS (1) Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710 USA

SO Biophysical Journal, (April, 1999) Vol. 76, No. 4, pp. 2090-2098. ISSN: 0006-3495.

DT Article

LA English

SL English

AB It has been established that the fusion of both biological membranes and phospholipid bilayers can be modulated by altering their lipid composition (Chernomordik et al., 1995. J. Membr. Biol. 146:3). In particular, when added exogenously between apposing membranes, monomyristoylphosphatidylcholine (MMPC) inhibits membrane fusion, whereas glycerol monoleate (GMO), oleic acid (OA), and arachidonic acid (AA) promote fusion. This present study uses x-ray diffraction to investigate the effects of MMPC, GMO, OA, and AA on the bending and stability of lipid

bilayers when bilayers are forced together with applied osmotic pressure. The addition of 10 and 30 mol% MMPC to egg phosphatidylcholine (EPC) bilayers maintains the bilayer structure, even when the interbilayer fluid spacing is reduced to apprx3 ANG, and increases the repulsive pressure between bilayers so that the fluid spacing in excess water increases by 5 and 15 ANG, respectively. Thus MMPC increases the undulation pressure, implying that the addition of MMPC promotes out-of-plane bending and decreases the adhesion energy between bilayers. In contrast, the addition of GMO has minor effects on the undulation pressure; 10 and 50 mol% GMO increase the fluid spacing of EPC in excess water by 0 and 2 ANG, respectively. However, x-ray diffraction indicates that, at small interbilayer separations, GMO, OA, or AA converts the bilayer to a structure containing hexagonally packed scattering units apprx50 ANG in diameter. Thus GMO, OA, or AA destabilizes bilayer structure as apposing bilayers are brought into contact, which could contribute to their role in promoting membrane fusion.

L8 ANSWER 16 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 2000:784091 CAPLUS
DN 134:331466
TI Polyphenols increase adhesion between lipid bilayers by forming interbilayer bridges
AU ***McIntosh, Thomas J.*** ; Pollastri, Michael P.; Porter, Ned A.; Simon, Sidney A.
CS Departments of Cell Biology, Duke University Medical Center, Durham, NC, 27710, USA
SO Basic Life Sci. (1999), 66(Plant Polyphenols 2), 451-470
CODEN: BLFSBY; ISSN: 0090-5542
PB Kluwer Academic/Plenum Publishers
DT Journal
LA English
AB The study summarizes the authors' work characterizing, at the mol. level, the interaction of tannic acid and related polyphenols with lipid bilayer vesicles.
RE.CNT 47
RE
(1) Baxter, N; Biochemistry 1997, V36, P5566 CAPLUS
(3) Boulanger, Y; Biochemistry 1981, V20, P6824 CAPLUS
(6) Ebihara, L; Biophys J 1979, V28, P185 CAPLUS
(7) Evans, E; Biophys J 1984, V46, P423 CAPLUS
(8) Evans, E; J Phys Chem 1987, V91, P4219 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 17 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1999:653113 CAPLUS
DN 132:32229
TI Structure and physical properties of the lipid membrane
AU ***McIntosh, Thomas J.***
CS Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710, USA
SO Curr. Top. Membr. (1999), 48(Membrane Permeability), 23-47
CODEN: CTMEET; ISSN: 1063-5823
PB Academic Press
DT Journal; General Review

LA English
AB A review with many refs. Because of the importance of the lipid bilayer as the structural core of biol. membranes, there has been sustained effort to understand the structure and phys. properties of phospholipid bilayers; this review summarizes some major findings in this area. Specific topics discussed include (1) phase behavior of membrane phospholipids; (2) structure of phospholipid bilayers; (3) stability and mech. properties of bilayers; (4) interbilayer interactions; and (5) roles of specific lipids in membrane bilayers. (c) 1999 Academic Press.
RE.CNT 226
RE
(1) Allen, T; Biochemistry 1990, V29, P2976 CAPLUS
(2) Asaoka, Y; Proc Natl Acad Sci U S A 1992, V89, P6447 CAPLUS
(3) Azzi, A; Eur J Biochem 1992, V208, P547 CAPLUS
(4) Baldwin, P; Biochemistry 1985, V24, P2633 CAPLUS
(5) Bazzi, M; Biochemistry 1991, V30, P7961 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1998:761797 CAPLUS
DN 130:17217
TI Vaccine against lipopolysaccharide core
IN Bennett-Guerrero, Elliott; Barclay, George Robin; Poxton, Ian Raymond; ***McIntosh, Thomas James*** ; Snyder, David Scott
PA Medical Defense Technologies, Llc, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9851217	A1	19981119	WO 1998-US9988	19980515
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874912	A1	19981208	AU 1998-74912	19980515
EP 1011440	A1	20000628	EP 1998-922339	19980515
R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				

PRAI US 1997-46680 P 19970516
WO 1998-US9988 W 19980515
AB Complete core LPS (lacking O-polysaccharide side chains) from Gram-neg. bacteria are incorporated into a vaccine typically in liposomes. The complete core of E. coli K 12 is particularly useful. Upon administration to a mammal the vaccine stimulates synthesis of antibodies which are cross-protective against smooth and rough forms of LPS from at least two different Gram-neg. bacterial strains having different core structures.
RE.CNT 9
RE

(1) Dale, P; The Journal of Infectious Diseases 1992, V166, P316 CAPLUS
(2) Dipadova, F; Infection and Immunity 1993, V61(9), P3863 CAPLUS
(3) Fang, I; Infection and Immunity 1993, V61(9), P3873 CAPLUS
(4) Green, S; Advances in Experimental Medicine and Biology 1995, V383, P83 CAPLUS
(6) Poxton, I; Journal of Immunological Methods 1995, V186, P1 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 19 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 11
AN 1998:473483 BIOSIS
DN PREV199800473483
TI A new monofluorinated phosphatidylcholine forms interdigitated bilayers.
AU Hirsh, Donald J.; Lazaro, Nancy; Wright, Lee R.; Boggs, Joan M.; ***McIntosh, Thomas J.*** ; Schaefer, Jacob; Blazyk, Jack (1)
CS (1) Dep. Chem. Biochem., Ohio Univ., Athens, OH 45701 USA
SO Biophysical Journal, (Oct., 1998) Vol. 75, No. 4, pp. 1858-1868. ISSN: 0006-3495.
DT Article
LA English
AB 16-Fluoropalmitic acid was synthesized from 16-hydroxypalmitic acid using diethylaminosulfur trifluoride. This monofluorinated fatty acid then was used to make 1-palmitoyl-2-(16-fluoropalmitoyl)-phosphatidylcholine (F-DPPC) as a fluorinated analog of dipalmitoylphosphatidylcholine (DPPC). Surprisingly, we found that the phase transition temperature (Tm) of F-DPPC occurs near 50degreeC, apprx 10degreeC higher than its nonfluorinated counterpart, DPPC, as judged by both differential scanning calorimetry and infrared spectroscopy. The pretransition observed for DPPC is absent in F-DPPC. A combination of REDOR, rotational-echo double-resonance, and conventional solid-state NMR experiments demonstrates that F-DPPC forms a fully interdigitated bilayer in the gel phase. Electron paramagnetic resonance experiments show that below Tm, the hydrocarbon chains of F-DPPC are more motionally restricted than those of DPPC. X-ray scattering experiments confirm that the thickness and packing of gel phase F-DPPC is similar to that of heptanetriol-induced interdigitated DPPC. F-DPPC is the first phosphoglyceride containing sn-1 and sn-2 ester-linked fatty acyl chains of equal length that spontaneously forms interdigitated bilayers in the gel state in the absence of inducing agents such as alcohols.

L8 ANSWER 20 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1998:700438 CAPLUS
DN 130:34530
TI Adsorption, molecular exchange and defect formation in membranes
AU Needham, David; ***McIntosh, Thomas J.*** ; Simon, Sidney A.; Zhelev, Doncho
CS Department of Mechanical Engineering and Materials Science, Duke University, Durham, NC, 27706, USA
SO Curr. Opin. Colloid Interface Sci. (1998), 3(5), 511-517 CODEN: COCSFL; ISSN: 1359-0294
PB Current Chemistry
DT Journal; General Review
LA English
AB A review with 56 refs. The past year has seen significant advances in our understanding of the key factors involved in detg. whether a macromol. or

colloidal particle can reach, bind to, and absorb into lipid bilayer membranes. The highlights include the need to combine both electrostatic and hydrophobic interactions to achieve stable binding, the influence of membrane dipoles, the mol.-scale filter provided by grafted polymers, and the recognition that surfactants and peptides form defects that depend on their aggregated state in the membrane.
RE.CNT 56
RE
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(2) Ben-Tal, N; Biophys J 1996, V71, P561 CAPLUS
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(5) Cafiso, D; Permeability and Stability of Lipid Bilayers 1995, P179 CAPLUS
(6) Chaloin, L; Biochemistry 1997, V36, P11179 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 21 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:335643 BIOSIS
DN PREV199800335643
TI Physical and biological properties of cationic phospholipids.
AU MacDonald, Robert C. (1); Rosenzweig, Howard S. (1); Rakhmanova, Vera A. (1); Choi, Kenneth L. (1); Tarahovsky, Yury S.; Kennedy, Michael T. (1); ***McIntosh, Thomas J.***
CS (1) Dep. Biochem. Molecular Biol. Cell Biol., Northwestern Univ., Evanston, IL 60208 USA
SO Biophysical Journal, (Feb., 1998) Vol. 74, No. 2 PART 2, pp. A310.
Meeting Info.: Forty-second Annual Meeting of the Biophysical Society Kansas City, Missouri, USA February 22-26, 1998
ISSN: 0006-3495.
DT Conference
LA English

L8 ANSWER 22 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1998:457608 BIOSIS
DN PREV199800457608
TI Surface chemistry of the sterically stabilized peg-liposome: General principles.
AU Needham, David (1); ***McIntosh, Thomas J.*** ; Zhelev, Doncho (1)
CS (1) Dep. Mechanical Engineering and Materials Sci., Duke Univ., Durham, NC 27706 USA
SO Journal of Liposome Research, (Feb., 1998) Vol. 8, No. 1, pp. 24-25.
Meeting Info.: Sixth Liposome Research Days Conference Les Embiez, France May 28-31, 1998
ISSN: 0898-2104.
DT Conference
LA English

L8 ANSWER 23 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 12
AN 1997:510242 BIOSIS
DN PREV199799809445
TI The effect of phloretin on the hydration of egg phosphatidylcholine multilayers.
AU Jendrasiak, Gordon L. (1); Smith, Ralph L.; ***McIntosh, Thomas J.***
CS (1) Dep. Radiol. Oncol., Sch. Med., East Carolina Univ., Leo Jenkins Cancer Cent., Greenville, NC 27858-4354 USA

SO Biochimica et Biophysica Acta, (1997) Vol. 1329, No. 1, pp. 159-168.
ISSN: 0006-3002.
DT Article
LA English
AB The effect of phloretin on the hydration, structure and interactive properties of supported phospholipid bilayers has been studied by a combination of direct water adsorption measurements and X-ray diffraction. Adsorption isotherms show that over a wide range of relative vapor pressures (from 0 to approximately 1.0) the addition of 20 or 40 mol% phloretin significantly alters the amount of water adsorbed by egg phosphatidylcholine (EPC) multilayers. X-ray diffraction analysis shows that the incorporation of phloretin decreases the width of the EPC bilayer, thereby increasing the area per lipid molecule from approximately 64 ANG -2 for EPC to about 78 ANG -2 for EPC:Ph, 3:2, M:M. Phloretin also decreases the distance between apposing EPC bilayers, most likely because it causes a reduction in repulsive hydration/steric pressure between apposing bilayers. Because phloretin decreases the fluid layer between bilayers by a larger amount than it increases the area per EPC molecule, phloretin has the effect of decreasing the water volume in the multilayers.

L8 ANSWER 24 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 13
AN 1996:528890 BIOSIS
DN PREV199699251246
TI Structure and interactive properties of highly fluorinated phospholipid bilayers.
AU ***McIntosh, Thomas J. (1)*** ; Simon, Sidney A.; Vierling, Pierre; Santaella, Catherine; Ravily, Veronique
CS (1) Dep. Cell Biol., Duke Univ. Med. Cent., Box 3011, Durham, NC 27710 USA
SO Biophysical Journal, (1996) Vol. 71, No. 4, pp. 1853-1868.
ISSN: 0006-3495.
DT Article
LA English
AB Because liposomes containing fluoroalkylated phospholipids are being developed for in vivo drug delivery, the structure and interactive properties of several fluoroalkylated glycerophosphocholines (PCs) were investigated by x-ray diffraction/osmotic stress, dipole potential, and hydrophobic ion binding measurements. The lipids included PCs with highly fluorinated tails on both alkyl chains and PCs with one hydrocarbon chain and one fluoroalkylated chain. Electron density profiles showed high electron density peaks in the center of the bilayer corresponding to the fluorine atoms. The height and width of these high density peaks varied systematically, depending on the number of fluorines and their position on the alkyl chains, and on whether the bilayer was in the gel or liquid crystalline phase. Wide-angle diffraction showed that in both gel and liquid crystalline bilayers the distance between adjacent alkyl chains was greater in fluoroalkylated PCs than in analogous hydrocarbon PCs. For interbilayer separations of less than about 8 ANG , pressure-distance relations for fluoroalkylated PCs were similar to those previously obtained from PC bilayers with hydrocarbon chains. However, for bilayer separations greater than 8 ANG , the total repulsive pressure depended on whether the fluoroalkylated PC was in a gel or liquid-crystalline phase. We argue that these pressure-distance relations contain contributions from both hydration and entropic repulsive pressures. Dipole potentials ranged

from -680 mV for PCs with both chains fluoroalkylated to -180 mV for PCs with one chain fluoroalkylated, compared to +415 mV for egg PC. The change in dipole potential as a function of subphase concentration of tetraphenyl-boron was much larger for egg PC than for fluorinated PC monolayers, indicating that the fluorine atoms modified the binding of this hydrophobic anion. Thus, compared to conventional liposomes, liposomes made from fluoroalkylated PCs have different binding properties, which may be relevant to their use as drug carriers.

L8 ANSWER 25 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1996:131171 CAPLUS
DN 124:168798
TI Adhesion between phosphatidylethanolamine bilayers
AU ***McIntosh, Thomas J.*** ; Simon, Sidney A.
CS Medical Center, Duke University, Durham, NC, 27710, USA
SO Langmuir (1996), 12(6), 1622-30
CODEN: LANGD5; ISSN: 0743-7463
DT Journal
LA English
AB The goal of this study is to provide addnl. information on the short-range interactions that det. the adhesion energy between bilayer surfaces. The specific problem concerns the hydration properties of bilayers of the membrane lipid phosphatidylethanolamine (PE), which imbibe much less water than bilayers composed of the other common zwitterionic membrane lipid, phosphatidylcholine (PC). The osmotic stress/X-ray diffraction method was used to measure pressure-distance relations for PE and PC bilayers contg. known mole fractions of the charged lipid phosphatidic acid (PA). The addn. of 20 mol % PA to either PC or PE bilayers swelled the bilayers by an amt. predictable from electrostatic double-layer theory. However, whereas the addn. of 5 mol % PA disjoined PC bilayers, it did not change the fluid space between PE bilayers. By calcg. the magnitude of the electrostatic pressure necessary to disjoin the bilayers, we est. the adhesion energy for gel phase PE bilayers to be about -0.7 erg/cm2, a value considerably larger than previously measured values for gel phase PC bilayers. The magnitude of the adhesion energy indicates that, in addn. to the attractive van der Waals pressure, there is another attractive pressure between adjacent PE layers that prevents them from swelling to the extent of PC bilayers. We argue that a small fraction of direct electrostatic interbilayer interactions or indirect hydrogen-bonded water interactions between the N+H3 group in one bilayer and the PO4- group in the apposing bilayers could account for the addnl. attractive interactions in PE bilayers.

L8 ANSWER 26 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1996:533253 CAPLUS
DN 125:240898
TI Short-range pressures between lipid bilayer membranes
AU ***McIntosh, Thomas J.*** ; Simon, Sidney A.
CS Department of Cell Biology, Duke University Medical Center, Durham, NC, 27710, USA
SO Colloids Surf., A (1996), 116(3), 251-268
CODEN: CPEAEH; ISSN: 0927-7757
DT Journal; General Review
LA English

AB A review with 121 refs. For many years a large, short-range repulsive interaction has been obsd. between a variety of hydrated surfaces. The phys. origin of this ubiquitous interaction has been controversial. In the case of lipid bilayers, proposed mechanisms include a hydration pressure, due to water polarization and/or hydrogen-bond reorientation by the bilayer surface, and several types of entropic (steric) pressures, due to motion of individual lipid mols. or undulations of the entire bilayer. This review focuses on a no. of recent osmotic stress/X-ray diffraction expts. performed with phosphatidylcholine bilayers designed to det. the distance range where each of these pressures dominates. At very short interbilayer sepns. (less than about 4 .ANG.), the pressure-distance curve depends on the vol. fraction of head groups at the interface, indicating the presence of a large steric barrier arising from direct interactions between head groups from opposing bilayers. The range of this steric pressure can be increased by the addn. of lipids with larger head groups, such as glycolipids or lipids with covalently attached polymers (polyethylene glycol lipids). For intermediate interbilayer sepns. (about 4-10 .ANG.), the pressure-distance curves are similar for liq.-cryst. and cryst. phosphatidylcholine bilayers, the pressure-fluid spacing relationship is nearly independent of temp., and the magnitude of the pressure depends on the dipole potential. In this range of fluid spacings we argue that the pressure can be best accounted for by a hydration pressure. For interbilayer spacing greater than about 10 .ANG., the magnitude and range of the obsd. pressure depend on temp. and on the bending modulus of the bilayer. These observations provide compelling evidence for the presence of a longer-range undulation pressure, that markedly influences the hydration properties of phospholipid bilayers.

L8 ANSWER 27 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 14
AN 1996:479556 BIOSIS
DN PREV199699194812
TI Hydration properties of lamellar and non-lamellar phases of phosphatidylcholine and phosphatidylethanolamine.
AU ***McIntosh, Thomas J.***
CS Dep. Cell Biol., Duke Univ. Med. Cent., Durham, NC 27710 USA
SO Chemistry and Physics of Lipids, (1996) Vol. 81, No. 2, pp. 117-131. ISSN: 0009-3084.
DT General Review
LA English
AB Two of the most common phospholipids in biological membranes are phosphatidylcholine (PC) and phosphatidylethanolamine (PE). Over a wide range of temperatures the PCs found in biological membranes form lamellar (bilayer) phases when dispersed in excess water, whereas PEs form either lamellar or hexagonal phases depending on their hydrocarbon chain composition. This paper details the hydration properties of lamellar and hexagonal phases formed by PCs and PEs, focusing on the energetics of hydration of these phases. For the hexagonal phase, the energy of bending the lipid monolayer is a critical term, with other contributions arising from the energies of hydrating the lipid headgroups and filling voids in the interstices in the hydrocarbon region. For the lamellar phase of PC, the water content is determined by a balance between the attractive van der Waals pressure and repulsive hydration and entropic (steric) pressures. In the case of PE bilayers, recent experiments demonstrate the presence of an additional strong, short-range attractive interaction,

possibly due to hydrogen-bonded water interactions between N+ H-3 groups in one bilayer and the PO-4- groups in the apposing bilayer, This additional attractive pressure causes apposing PE bilayers to adhere strongly and to imbibe considerably less water than PC bilayers.

L8 ANSWER 28 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1995:868141 CAPLUS
DN 123:296438
TI Effect of Bilayer Composition on the Phase Behavior of Liposomal Suspensions Containing Poly(ethylene glycol)-Lipids
AU Hristova, Kalina; Kenworthy, Anne; ***McIntosh, Thomas J.***
CS Department of Mechanical Engineering and Materials Science, Duke University, Durham, NC, 27708, USA
SO Macromolecules (1995), 28(23), 7693-9
CODEN: MAMOBX; ISSN: 0024-9297
DT Journal
LA English
AB Liposomes contg. phospholipids with covalently attached poly(ethylene glycol) (PEG-lipids) are being developed for use as carriers in in vivo drug delivery. A crit. design parameter for these liposomes is the max. amt. of PEG-lipids that can be incorporated into the phospholipid bilayer before it is converted into a micelle. In this paper, X-ray diffraction is used to det. this satn. limit of PEG-lipids for a variety of phospholipid bilayers with different tensile strengths and polymorphic properties. It is found that 15-20 mol % PEG-lipid can be incorporated into gel phase bilayers, liq.-cryst. bilayers, and bilayers contg. equimolar cholesterol. However, the satn. limit of PEG-lipid in the bilayer is decreased to about 8 mol % when lysolipids are added to liq.-cryst. phase bilayers or when the gel phase bilayers are made with shorter hydrocarbon chains. These data indicate that the phase transition from lamellar to micellar phase for lipid suspensions contg. PEG-lipids does not depend strongly on the tensile strength of the bilayer, but rather is detd. primarily by the polymorphic properties of the lipid mols. This study also measures the range and magnitude of the steric barrier provided by the incorporation of PEG-lipid into bilayers of different compns. The steric barrier depends on the concn. of PEG-lipid in the bilayer, with the incorporation of 10 mol % PEG-2000 into gel, liq.-cryst., and cholesterol-contg. bilayers providing a barrier that extends about 65 .ANG. from each bilayer surface.

L8 ANSWER 29 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:369258 BIOSIS
DN PREV199497382258
TI Hydration and steric pressures between phospholipid bilayers.
AU ***McIntosh, Thomas J. (1)*** ; Simon, Sidney A.
CS (1) Dep. Cell Biol., Duke Univ. Med. Cent., Durham, NC 27710 USA
SO Stroud, R. M. [Editor]. Annual Review of Biophysics and Biomolecular Structure, (1994) Vol. 23, pp. 27-51. Annual Review of Biophysics and Biomolecular Structure.
Publisher: Annual Reviews Inc. P.O. Box 10139, 4139 El Camino Way, Palo Alto, California 94306, USA.
ISSN: 1056-8700. ISBN: 0-8243-1823-4.
DT Book; General Review
LA English

L8 ANSWER 30 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 15
AN 1994:489834 BIOSIS
DN PREV199497502834
TI Long- and short-range interactions between phospholipid/ganglioside GM1 bilayers.
AU ***McIntosh, Thomas J. (1)*** ; Simon, Sidney A.
CS (1) Dep. Cell Biol. Neurobiol. Anesthesiol., Duke University Med. Center, Durham, NC 27710 USA
SO Biochemistry, (1994) Vol. 33, No. 34, pp. 10477-10486.
ISSN: 0006-2960.
DT Article
LA English
AB The structure and interactive properties of liquid-crystalline egg phosphatidylcholine (EPC) bilayers containing the ganglioside GM1 and its uncharged analogue, asialoGM1 (AGM1), have been obtained by X-ray diffraction analysis of osmotically stressed liposomes. Both electron density profiles and reciprocal space modeling indicate that (1) the incorporation of up to 30 mol % GM1 into EPC bilayers has little effect on bilayer organization and (2) the oligosaccharide portion of the GM1 molecule extends at least 12 ANG beyond the EPC head group into the fluid space, implying that the GM1 head group is nearly fully extended from the bilayer surface. Pressure-distance relations for EPC:GM1 bilayers in 100 mM ionic strength buffer show that, for large bilayer separations, the interbilayer repulsive pressure decays exponentially with a decay length and magnitude expected for electrostatic repulsion arising from the charged GM1. However, at interbilayer separations of ltoreq 30 ANG for 7:3 and 8:2 EPC:GM1 and ltoreq 22 ANG for 9:1 EPC:GM1, the pressure-distance curves have distinct upward breaks, with the sharpness of this break depending strongly on the amount of GM1 in the bilayer For 7:3 EPC:GM1 bilayers, the break is quite sharp so that the distance between bilayers does not decrease below 28 ANG with further increases in applied pressure. For EPC:GM1 8:2 and 9:1 bilayers, the upward break becomes softer with decreasing GM1 concentration. For uncharged EPC:AGM1 bilayers, the repulsive pressure extends only to an equilibrium fluid separation of about 36 ANG , but has a similar behavior to the pressure-distance data for EPC:GM1 for separations below 20 ANG . We argue that the nonelectrostatic repulsive pressures arise primarily from the steric interactions between the hydrated oligosaccharide head groups that protrude from the bilayer surface.

L8 ANSWER 31 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:185310 BIOSIS
DN PREV199497198310
TI Infection control in the Russian Federation: Review of a tertiary care hospital.
AU Nettleman, Mary D. (1); McIntosh, Sandra L.; ***McIntosh, Thomas J.*** ; Wenger, Jan; Geerdes, Heidi
CS (1) C42 GH, Univ. Iowa Coll. Med., 200 Hawkins Drive, Iowa City, IA 52242 USA
SO Infection Control and Hospital Epidemiology, (1994) Vol. 15, No. 3, pp. 200-202.
ISSN: 0899-823X.
DT Article

LA English

L8 ANSWER 32 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1995:20275 CAPLUS
DN 122:49138
TI Hydration and steric pressures between phospholipid bilayers
AU ***McIntosh, Thomas J.*** ; Simon, Sidney A.
CS Medical Center, Duke Univ., Durham, NC, 27710, USA
SO Annu. Rev. Biophys. Biomol. Struct. (1994), 23, 27-51
CODEN: ABBSE4; ISSN: 1056-8700
DT Journal; General Review
LA English
AB A review with 89 refs. of models for short-range repulsion between bilayers, methods, and pressure-distance data.

L8 ANSWER 33 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 16
AN 1994:457374 BIOSIS
DN PREV199497470374
TI Colloid osmotic pressure of steer alpha- and beta-crystallins: Possible functional roles for lens crystallin distribution and structural diversity.
AU Kenworthy, Anne K.; Magid, Alan D. (1); Oliver, Timothy N.; ***McIntosh,*** *** Thomas J. (1)***
CS (1) Associated Regulatory Consultants Inc., PO Box 12262, Research Triangle Park, NC 27709 USA
SO Experimental Eye Research, (1994) Vol. 59, No. 1, pp. 11-30.
ISSN: 0014-4835.
DT Article
LA English
AB This study addresses the general mechanisms whereby the major cytoplasmic proteins from the adult bovine tens contribute both to transparency and maintenance of the refractive index gradient across the lens. Colloid osmotic properties and quaternary structure were measured for alpha and beta-crystallins isolated from the steer tens, including low-molecular-weight crystallins from the cortex (a-Lc and beta-L) and nucleus (alpha-Ln) and high-molecular-weight crystallins from the nucleus (alpha-H and beta-L). In electron microscopic images of rotary-shadowed preparations alpha-Lc appears as spherical particles 16 nm in diameter, alpha-Ln appeared as individual spheres or small aggregates of spherical subunits, alpha-H contained large irregular aggregates as large as 180 nm, and both beta-1 and beta-H appeared as elliptical particles of 7-9 nm diameter. Secondary osmometry showed that for all these crystallins colloid osmotic pressure increased monotonically in a non-linear fashion with protein concentration. For the alpha-crystallins, osmotic pressure rose more steeply with concentration for alpha-Lc than for either alpha-Ln or alpha-H, so that at 0.3 g ml-1 at 0.1 m ionic strength, the colloid osmotic pressure of and alpha-Ln were approximately 2.6 times 10-5 dyn cm-2, 1.6 times 10-5 dyn cm-2 and 1.0 times 10-5 dyn cm-1, respectively. In a similar manner, osmotic pressure rose more steeply with concentration of beta-L, than for beta-H so that at 0.3 g ml-1 at 0.1 m ionic strength the colloid osmotic pressures of beta-L, and beta-H were 2.6 times 10-3 dyn cm-2 and 1.1 times 10-5 dyn cm-2, respectively. The osmotic pressure of alpha-Lc dropped as ionic strength was increased from 0.02 to 0.4 M. For beta-L, and beta-H, osmotic pressure dropped as ionic strength was

increased from 0.0.2 to 0.1 m but was nearly the same at 0.1 M and 0.4 M ionic strength. The data for steer alpha-Ln and beta-H were similar to previous reports for calf cortical alpha-L and beta-crystallins, respectively. The osmotic pressure isotherms for alpha-Lc and that previously reported for steer cortical extract were nearly identical, whereas the nuclear crystallins (alpha-Ln, alpha-H or beta-H) generated slightly higher pressures than those previously reported for steer nuclear crystallin extracts. In all cases. osmotic pressure rose more steeply with concentration for the cortical crystallins than for the nuclear crystallins. Calculations showed that the measured osmotic pressures generated by solutions of beta-L, and beta-H were similar to those predicted to arise from excluded volume effects in solutions of uncharged spherical proteins of 60 and 200 kDa, respectively. In contrast, the osmotic pressures generated by each of the alpha-crystallins were substantially larger than those predicted for pure excluded volume effects between uncharged spherical proteins, pointing to a role for Donnan osmotic pressure and electrostatic repulsion in defining alpha-crystallin interactions. In particular, modeling studies indicated that the osmotic properties of alpha-Lc and alpha-Ln are consistent with the behavior of charged 750-kDa spheres, where a-H behaves as charged cylindrical particles. The comparison of the pressure isotherms of the isolated alpha- and beta-crystallins with the nuclear and cortical extracts suggests that the osmotic properties of the lens cytoplasm depend importantly on both the alpha and beta-crystallins, and implies that the gamma-crystallins also contribute to the osmotic properties of the nuclear cytoplasm. The unexpected similarities of the pressure isotherms of the crystallins within the cortex (alpha-L and beta-L) or nucleus (alpha-Ln, alpha-H and beta-H) are interpreted as arising from compensatory variations in the size, shape and charge of the proteins and are hypothesized to promote both transparency and the miscibility of the crystallin species in tens fiber cells. The differences in the pressure-concentration isotherms of the cortical and nuclear alpha- and beta-crystallins support the hypothesis that the spatial distribution of these proteins within the lens functions to maintain the radial gradient in refractive index that is essential to visual acuity.

L8 ANSWER 34 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 17
AN 1993:474168 BIOSIS
DN PREV199396107768
TI Contributions of hydration and steric (entropic) pressures to the interactions between phosphatidylcholine bilayers: Experiments with the subgel phase.
AU ***McIntosh, Thomas J. (1)*** ; Simon, Sidney A.
CS (1) Dep. Cell Biol. and Neurobiol. and Anesthesiol., Duke Univ. Med. Cent., Durham, North Carolina 27710 USA
SO Biochemistry, (1993) Vol. 32, No. 32, pp. 8374-8384.
ISSN: 0006-2960.
DT Article
LA English
AB The total repulsive interaction between electrically neutral, fluid bilayer membranes is thought to have a number of components, including a hydration pressure, due to the reorientation of water by the bilayer, and steric (entropic) pressures due to bilayer undulations, head group motion, and molecular protrusions. For fully hydrated, crystalline bilayers these

three steric pressures should be relatively small, and the major repulsive pressure present should be the hydration pressure. Therefore, to isolate the contribution of hydration pressure to the total interbilayer interaction, we have measured pressure-distance data by X-ray diffraction analysis of osmotically stressed dipalmitoylphosphatidylcholine (DPPC) multilayers in the subgel phase, where wide-angle and low-angle X-ray data show the bilayers are crystalline. As applied pressure was increased from 0 to 1 times 10-6 dyn/cm-2 , the interbilayer fluid space (d-f) decreased less than 1 from its value at full hydration of 8.4 ANG . As the pressure was increased from 1 times 10-6 to 3 times 10-7 dyn/cm-2, d-f decreased from about 8 to 4 A. For this range of d-f, the repulsive pressure decayed exponentially with d-f with a decay length of 1.4 ANG . Further increases in applied pressure did not appreciably decrease d-f, so that there was a sharp upward break in the pressure-distance curve at an interbilayer spacing of about 3 ANG . in contrast, pressure-distance relations for gel (L-beta,) phase and liquid-crystalline (L-alpha) phase bilayers had much softer upward breaks at d-f lt 5 ANG and extended to larger d-f at zero applied pressure. However, the pressure-distance curves for all three phases decayed exponentially with approximately the same decay length for 4 lt d-f lt 8 ANG . We interpret these data to mean the following: (1) the repulsion observed for d-f lt 5 ANG is primarily a steric pressure whose range depends on head group motion; (2) the steric undulation pressure plays an important role in determining the hydration properties and the range of the total repulsive pressure for fluid membranes; (3) the same underlying mechanisms govern the repulsive pressure for all phases for 4 lt d-f lt 8 ANG ; (4) these mechanisms include a pressure due to reorientation of water molecules; and (5) the hydration pressure component extents a maximum of about two water molecules from the bilayer surface for the subgel phase.

L8 ANSWER 35 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1994:25631 CAPLUS
DN 120:25631
TI Phospholipid hydration
AU ***Mcintosh, Thomas J.*** ; Magid, Alan D.
CS Med. Cent., Duke Univ., Durham, NC, USA
SO Phospholipids Handb. (1993), 553-77. Editor(s): Cevc, Gregor. Publisher: Dekker, New York, N. Y.
CODEN: 59KHAT
DT Conference; General Review
LA English
AB A review, with over 100 refs. on the hydration properties of various phospholipids and membranes.

L8 ANSWER 36 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1992:124207 CAPLUS
DN 116:124207
TI Modulation of poly(ethylene glycol)-induced fusion by membrane hydration: importance of interbilayer separation
AU Burgess, Stephen W.; ***McIntosh, Thomas J.*** ; Lentz, Barry R.
CS Dep. Biochem., Univ. North Carolina, Chapel Hill, NC, 27599-7260, USA
SO Biochemistry (1992), 31(10), 2653-61
CODEN: BICHAW; ISSN: 0006-2960
DT Journal

LA English
AB Large unilamellar vesicles composed of lipids with different hydration properties were prepd. by the extrusion technique. Vesicles were composed of dioleoylphosphatidylcholine in combination with either 0.5 mol % monooleoylphosphatidylcholine or different molar ratios of dilauroylphosphatidylethanolamine. Fusion was revealed via a fluorescence assay for contents mixing and leakage, a fluorescent lipid probe assay for membrane mixing, and quasielastic light scattering to detect vesicle size growth. As the percentage of poorly hydrating phosphatidylethanolamine increased, the concn. of PEG required to induce fusion decreased. From differential scanning calorimetry studies of membrane-phase behavior and x-ray diffraction monitoring of phase structure in PEG, it was concluded that PEG did not induce a hexagonal-phase transition of lamellar-phase sepn. Electron d. profiles derived from x-ray diffraction studies of multi- and unilamellar vesicles indicated that the water layer between vesicles had a thickness of approx. 5 .ANG. at PEG concns. at which vesicles were first induced to fuse. At this distance of sepn., the choline headgroups from apposing bilayers are in near-mol. contact. Since pure phosphatidylcholine vesicles did not fuse at this interbilayer spacing, a redn. in the interbilayer water layer to a crit. width of .apprx.2 water mols. may contribute to but is not sufficient to produce PEG-mediated fusion of phospholipid membranes. Comparison of these results with other results from this lab. also indicates that, while close contact between bilayers promotes fusion, near-mol. contact is apparently not absolutely necessary to bring about fusion. A tentative model is presented to account for these results.

L8 ANSWER 37 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1992:101417 CAPLUS
DN 116:101417
TI Interbilayer interactions between sphingomyelin and sphingomyelin/cholesterol bilayers
AU ***McIntosh, Thomas J.*** ; Simon, Sidney A.; Needham, David; Huang, Ching Hsien
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biochemistry (1992), 31(7), 2020-4
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Pressure vs. fluid spacing relations have been obtained for sphingomyelin bilayers in the gel phase and equimolar sphingomyelin/cholesterol in the liq.-cryst. phase by the use of X-ray diffraction anal. of osmotically stressed aq. dispersions and oriented multilayers. For interbilayer sepns. in the range of 5-20 .ANG., the repulsive hydration pressure decays exponentially with increasing fluid spacing. The decay length (.lambda.) of this repulsive pressure is about 2 .ANG. for both bovine brain and N-tetracosanoylspingomyelin, similar to that previously found for phosphatidylcholine bilayers. However, both the magnitude of the hydration pressure and the magnitude of the dipole potential (V) measured for monolayers in equil. with liposomes are considerably smaller for sphingomyelin than for either gel or liq.-cryst. phosphatidylcholine bilayers. Addn. of equimolar cholesterol increases both the magnitude of the hydration pressure and the dipole potential. These data suggest that the magnitude of the hydration pressure depends on the elec. field at the

interface as given by (V/.lambda.)2. For sphingomyelin bilayers, there is a sharp upward break in the pressure-fluid spacing relation at an interbilayer spacing of about 5 .ANG., indicating the onset of steric hindrance between the head groups of apposing bilayers.

L8 ANSWER 38 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1992:101418 CAPLUS
DN 116:101418
TI Structure and cohesive properties of sphingomyelin/cholesterol bilayers
AU ***McIntosh, Thomas J.*** ; Simon, Sidney A.; Needham, David; Huang, Ching Hsien
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biochemistry (1992), 31(7), 2012-20
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Thermal, structural, and cohesive measurements have been obtained for both bovine brain sphingomyelin (BSM) and N-tetracosanoylsphingomyelin (C24-SM) in the presence and absence of cholesterol. A goal of these expts. has been to clarify the mechanisms responsible for the strong interaction between sphingomyelin and cholesterol. Differential scanning calorimetry shows that fully hydrated bilayers of BSM and C24-SM have main endothermic phase transitions at 39.degree. and 46.degree., resp., that reflect the melting of the acyl chains from a gel to a liq.-cryst. phase. For each lipid, the addn. of cholesterol monotonically reduces the enthalpy of this transition, so that at equimolar cholesterol the transition enthalpy is zero. The addn. of equimolar cholesterol to either BSM or C24-SM converts the wide-angle X-ray diffraction reflection at 4.15 .ANG. to a broad band centered at 4.5 .ANG.. Electron d. profiles of gel-phase C24-SM bilayers contain two terminal Me dips in the center of the bilayer, indicating that the lipid hydrocarbon chains partially interdigitate so that the long satd. 24-carbon acyl chains in one monolayer cross the bilayer center and appose the shorter sphingosine chains from the other monolayer. The incorporation of cholesterol adds electron d. to the hydrocarbon chain region near the head group and removes the double terminal Me dip. These wide- and low-angle X-ray data indicate that cholesterol packs into the hydrocarbon chain region near the sphingomyelin head group, fluidizes the methylene chains near the center of the bilayer compared to the gel phase, and reduces the extent of methylene chain interdigitation. This redn. of chain interdigitation by cholesterol could reduce the possibility of energetically unfavorable voids in the center of biol. membranes that contain sphingomyelin. Isothermal compressibility moduli are similar for bilayers composed of equimolar cholesterol and either BSM, C24-SM, or satd. long-chain phosphatidylcholines but are significantly higher than published values for equimolar cholesterol with unsatd. phosphatidylcholines. These compressibility data suggest that the strong interaction between sphingomyelin and cholesterol arises from the van der Waals interactions between cholesterol and satd. lipid acyl chains and that there is no specific hydrogen-bond formation between cholesterol and sphingomyelin. Although the acyl chain of BSM may contain a double bond, it is argued that BSM interacts strongly with cholesterol because the principle unsatd. fatty acid of BSM (nervonic acid) has its cis double bond at the 15 position, which is far enough down the chain to not affect the cholesterol-acyl chain interaction.

L8 ANSWER 39 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1992:189865 CAPLUS
DN 116:189865
TI Modulation of the interbilayer hydration pressure by the addition of dipoles at the hydrocarbon/water interface
AU Simon, Sidney A.; ***McIntosh, Thomas J.*** ; Magid, Alan D.; Needham, David
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biophys. J. (1992), 61(3), 786-99
CODEN: BIOJAU; ISSN: 0006-3495
DT Journal
LA English
AB The effects of the cholesterol analog 5.alpha.-cholestan-3.beta.-ol-6-one (6-ketocholestanol) on bilayer structure, bilayer cohesive properties, and interbilayer repulsive pressures have been studied by a combination of x-ray diffraction, pipet aspiration, and dipole potential expts. It is found that 6-ketocholesterol, which has a similar structure to cholesterol except with a keto moiety at the 6-position of the B ring, has quite different effects than cholesterol on bilayer organization and cohesive properties. Unlike cholesterol, 6-ketocholestanol does not appreciably modify the thickness of liq.-cryst. egg phosphatidylcholine (EPC) bilayers, and causes a much smaller increase in bilayer compressibility modulus than does cholesterol. These data imply that 6-ketocholestanol has both its hydroxyl and keto moieties situated near the water-hydrocarbon interface thus making its orientation in the bilayer different from cholesterol's. The addn. of equimolar 6-ketocholestanol into EPC bilayers increases the magnitude, but not the decay length, of the exponentially decaying repulsive hydration pressure between adjacent bilayers. Incorporation of equimolar 6-ketocholestanol into EPC monolayers increases the dipole potential by .apprx.300 mV. These data are consistent with previous observation that the magnitude of the hydration pressure is proportional to the square of the dipole potential. These results mean that 6-ketocholestanol, despite its location in the bilayer hydrocarbon region, .apprx.10.ANG. from the phys. edge of the bilayer, modifies the organization of interlamellar water. It was assumed that the incorporation of 6-ketocholestanol into EPC bilayers increases the hydration pressure, at least in part, by increasing the elec. field strength in the polar head group region.

L8 ANSWER 40 OF 66 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 18
AN 1993:57389 BIOSIS
DN PREV199395033691
TI Colloid osmotic pressure of steer crystallins: Implications for the origin of the refractive index gradient and transparency of the lens.
AU Magid, Alan D.; Kenworthy, Anne K.; ***McIntosh, Thomas J. (1)***
CS (1) Dep. Cell Biology, Duke Univ. Med. Cent., Durham, N.C. 27710 USA
SO Experimental Eye Research, (1992) Vol. 55, No. 4, pp. 615-627.
ISSN: 0014-4835.
DT Article
LA English
AB The osmotic behavior of soluble cortical and nuclear steer lens crystallins was characterized by secondary osmometry for several ionic strength and pH conditions. Osmotic pressure versus protein concentration

relationships were measured for pressures up to 1.15 times 10-6 dyn cm-2. At low concentrations (lt 0.2 g ml-1), the osmotic pressure increased linearly with pressure, whereas for concentrations above 0.2 g ml-1, the pressure rose more sharply, giving progressively larger changes in osmotic pressure with increasing crystallin concentration. At a given ionic strength and applied osmotic pressure, the nuclear proteins attained a higher protein concentration than did the cortical proteins. For example, at the highest osmotic pressure of 1.15 times 10-6 dyn cm-2 at pH 7.6 and 0.1 M ionic strength, the observed protein concentrations were 0.43 g ml-1 for the cortical proteins and 0.52 g ml-1 for the nuclear proteins. For both cortical and nuclear steer crystallins, the pressure rose more steeply with concentration than do pressures for calf crystallins described in the literature. The impact of these developmental differences in osmotic pressure on lens transparency is discussed. Both the nuclear and cortical crystallins exhibited ionic strength-dependent shifts in their pressure-concentration behavior. At 0.02 M ionic strength, higher pressures were observed, whereas at 0.4 M ionic strength lower pressures were observed for a given protein concentration. The crystallins were also found to equilibrate to different protein concentrations at a constant osmotic pressure and 0.1 M ionic strength over a pH range of 4-9, with a maximum concentration around pH 5 for the cortical crystallins and pH 6 for the nuclear crystallins. Thus, the adult bovine cortical and nuclear soluble lens extracts are different in their osmotic properties, reflecting underlying differences in protein composition. The results of the ionic strength and pH experiments suggest that hard-sphere, electrostatic, and Donnan forces contribute to the total colloid osmotic pressure of the lens crystallins. However, near physiologic pH and ionic strength the charges of the proteins are screened to the extent that the colloid osmotic pressure exhibits only minor changes for large changes in ionic conditions. The differences in the osmotic behavior of the cortical and nuclear proteins are consistent with a model where regional variations in the colloid osmotic properties of the proteins across the lens help support the radial refractive index gradient that is present in vertebrate lenses. The importance of a radial concentration gradient of metabolites is also discussed.

L8 ANSWER 41 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1992:443715 CAPLUS
DN 117:43715
TI The electrical conductivity of phospholipid films as an iodine-sensing mechanism
AU Jendrasiak, Gordon L.; Madison, Gregory E.; Smith, Ralph; ***McIntosh,*** *** Thomas J.***
CS Sch. Med., East Carolina Univ., Greenville, NC, 27858-4354, USA
SO Biosens. Bioelectron. (1992), 7(4), 291-300
CODEN: BBIOE4; ISSN: 0956-5663
DT Journal
LA English
AB The d.c. elec. cond. of dry phospholipid films is increased by some 8-11 orders of magnitude by the adsorption of iodine vapor. The cond. of these films has been found to increase as a function of iodine vapor pressure and the quant. relationship between elec. cond. and the adsorbed iodine has been detd. Films composed of phospholipids with unsatd. hydrocarbon chains are some three orders of magnitude more elec. conductive than are

films of phospholipids contg. satd. hydrocarbon chains. Optical spectroscopic measurements show the development of absorption bands centered near 294 nm and 365 nm, upon iodine adsorption. These bands are much more intense for unsatd. phospholipids than for satd. ones. X-ray diffraction studies show that exposure to iodine decreases the thickness of phospholipid bilayers contg. unsatd. hydrocarbon chains but does not change the thickness of bilayers contg. only satd. chains. The elec. response of the lipid films, upon exposure to iodine, suggests their possible use as iodine sensors.

L8 ANSWER 42 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1992:480849 CAPLUS
DN 117:80849
TI The effect of adsorbed iodine on the electrical conductivity of phospholipid films
AU Jendrasiak, Gordon L.; ***McIntosh, Thomas J.*** ; Madison, Gregory E.; Smith, Ralph
CS Sch. Med., East Carolina Univ., Greenville, NC, USA
SO Charge Field Eff. Biosyst.--3, [Int. Symp.], 3rd (1992), Meeting Date 1991, 53-67. Editor(s): Allen, Milton J. Publisher: Birkhaeuser, Boston, Mass.
CODEN: 57VVAA
DT Conference
LA English
AB The elec. conduction of dry films formed from EPC, DPPC, and other phospholipids was measured as a function of I adsorbed. This elec. cond. is related to the magnitude of the 294 and 365 optical absorption bands developed upon I adsorption by EPC and by DPPC films. The absorption bands are tentatively ascribed to the presence of I3-. Since the hydrocarbon chains in EPC have considerable unsatn., whereas those in DPPC are completely unsatd., the effect of unsatn. on the I-induced elec. cond. has thus been measured. X-ray diffraction techniques were also used to study the structural effect I has on films from both these phosphatidylcholines, as well as DC8,9PC, and there is a correlation of the structure and elec. behavior of the films.

L8 ANSWER 43 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1991:160284 CAPLUS
DN 114:160284
TI The hydration pressure between lipid bilayers. Comparison of measurements using x-ray diffraction and calorimetry
AU Simon, Sidney A.; Fink, Cynthia A.; Kenworthy, Anne K.; ***McIntosh,*** *** Thomas J.***
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biophys. J. (1991), 59(3), 538-46
CODEN: BIOJAU; ISSN: 0006-3495
DT Journal
LA English
AB The hydration pressure between dipalmitoylphosphatidyl-N,N-dimethylethanolamine (DPPE-Me2) bilayers has been analyzed by both x-ray diffraction measurements of osmotically stressed liposomes and by differential scanning calorimetry. By the x-ray method, a magnitude (Po) and decay length (.lambda.) were obtained for the hydration pressure which are both quite similar to those found for bilayers of other zwitterionic

lipids, such as phosphatidylcholines. I.e., x-ray anal. of DPPE-Me2 in the gel phase gives .lambda. = 1.3 .ANG., the same as that previously measured for the analogous gel phase lipid dipalmitoylphosphatidylcholine (DPPC), and Po = 3.9 .times. 109 dyn/cm2, which is in excellent agreement with the value of 3.6 .times. 109 dyn/cm2 calcd. from the measured Volta potential of DPPE-Me2 monolayers in equil. with liposomes. These results indicate that the removal of one Me group to convert DPPC to DPPE-Me2 does not markedly alter the range or magnitude of the hydration pressure. Calorimetry shows that the main gel to liq.-cryst. phase transition temp. of DPPE-Me2 is approx. const. for water contents ranging from 80 to 10 water mols. per lipid mol., but increases monotonically with decreasing water content below 10 waters per lipid. A theor. fit to these temp. vs. water content data predicts .lambda. = 6.7 .ANG.. The difference in obsd. values of .lambda. for x-ray and calorimetry measurements can be explained by effects on the thermograms of addnl. intra- and intermol. interactions which occur at low water contents where apposing bilayers are in contact. Thus, although calorimetry provides important data on the energetics of bilayer hydration, it is difficult to obtain quant. information on the hydration pressure from this technique.

L8 ANSWER 44 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1992:485303 CAPLUS
DN 117:85303
TI Short-range repulsive interactions between the surfaces of lipid membranes
AU ***McIntosh, Thomas J.*** ; Magid, Alan D.; Simon, Sidney A.
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Cell Model Membr. Interact., [Proc. Symp.] (1991), Meeting Date 1990, 249-65. Editor(s): Ohki, Shinpei. Publisher: Plenum, New York, N. Y. CODEN: 57WWAI
DT Conference; General Review
LA English
AB A review, with 59 refs., on the two principal short-range repulsive interactions acting between cell and model membranes, namely hydration and steric pressures.

L8 ANSWER 45 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1991:403542 CAPLUS
DN 115:3542
TI Surface ripples cause the large fluid spaces between gel phase bilayers containing small amounts of cholesterol
AU Simon, Sidney A.; ***McIntosh, Thomas J.***
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biochim. Biophys. Acta (1991), 1064(1), 69-74
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB Previous studies have found that small concns. of cholesterol, or several other mols. such as benzene and asialoganglioside, dramatically increase the fluid sepn. between gel phase phosphatidylcholine bilayers. These observations can not be explained in terms of changes in the repulsive and attractive pressures known to exist between flat gel phase bilayer surfaces. Here it is shown that the increase in fluid space occurs as a consequence of cholesterol inducing large periodic ripples in the plane of the bilayer. The anal. of K. Mortensen et al. (1988) indicates that the

sides of the ripples primarily contain gel phase phosphatidylcholine, whereas the apices are enriched in cholesterol and are liq.-cryst. Here it is argued that the large fluid spaces can be explained by steric repulsion between adjacent bilayers caused both by thermally induced accordion-like motions of these ripples and defects in the ripple organization. In addn., ripples potentially can decrease van der Waals attraction and change hydration repulsion between bilayers.

L8 ANSWER 46 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1990:520675 CAPLUS
DN 113:120675
TI Amiodarone-liposome interaction: a multinuclear NMR and x-ray diffraction study
AU Jendrasiak, Gordon L.; ***McIntosh, Thomas J.*** ; Ribeiro, Anthony; Porter, R. Stephen
CS Dep. Radiat. Oncol., East Carolina Univ., Greenville, NC, 27858-4354, USA
SO Biochim. Biophys. Acta (1990), 1024(1), 19-31
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB Amiodarone (I), a potent antiarrhythmic drug, is widely used in cardiol. Its electrophysiol. effects, as well as many of its side effects, seem to involve lipids. A multinuclear NMR and x-ray diffraction study of I in egg phosphatidylcholine (EPC) liposomes and lipid multilayers was reported. In proton NMR expts., I alters the signal from the lipid tri-Me ammonium group for pH values ranging from 3.2 to 8.4; cholesterol does not cause this alteration. The addn. of SCN- changes both the proton and phosphorus NMR spectra of liposomes contg. I. For both proton and carbon NMR, I modifies the signal from the lipid methylene groups, but to a far lesser extent than does cholesterol. Incorporation of I in EPC bilayers also modifies the low-angle x-ray diffraction patterns, decreasing the lamellar repeat period at low water contents, but swelling the fluid spaces between bilayers at high water contents. Electron d. profiles and modeling studies using the x-ray data indicate that I decreases the bilayer thickness and adds electron d. at the interfacial region of the bilayer. Anal. of the NMR and x-ray data indicates that the iodine atoms of I are located near the hydrocarbon/water interface and that the tertiary amine of I is in the headgroup region of the bilayer.

L8 ANSWER 47 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1989:529355 CAPLUS
DN 111:129355
TI Range of the solvation pressure between lipid membranes: dependence on the packing density of solvent molecules
AU ***McIntosh, Thomas J.*** ; Magid, Alan D.; Simon, Sidney A.
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biochemistry (1989), 28(19), 7904-12
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Well-ordered multilamellar arrays of liq.-cryst. phosphatidylcholine and equimolar phosphatidylcholine-cholesterol bilayers were formed in the nonaq. solvents formamide and 1,3-propanediol. The organization of these bilayers and the interactions between apposing bilayer surfaces were

investigated by x-ray diffraction anal. of liposomes compressed by applied osmotic pressures .ltoreq.6 .times. 107 dyn/cm2 (60 atm). The structure of egg phosphatidylcholine (EPC) bilayers in these solvents is quite different than in H2O, with the bilayer thickness being largest in H2O, 3 .ANG. narrower in formamide, and 6 .ANG. narrower in 1,3-propanediol. The incorporation of equimolar cholesterol increases the thickness of EPC bilayers immersed in each solvent, by >10 .ANG. in the case of 1,3-propanediol. The osmotic pressures of various concns. of the neutral polymer poly(vinylpyrrolidone) dissolved in formamide or 1,3-propanediol were measured with a custom-built membrane osmometer. These measurements are used to obtain the distance dependence of the repulsive solvation pressure between apposing bilayer surfaces. For each solvent, the solvation pressure decreases exponentially with distance between bilayer surfaces. However, for both EPC and EPC-cholesterol bilayers, the decay length and magnitude of this repulsive pressure strongly depend on the solvent. The decay length for EPC bilayers in H2O, formamide, and 1,3-propanediol is 1.7, 2.4, and 2.6 .ANG., resp., whereas the decay length for equimolar EPC-cholesterol bilayers in H2O, formamide, and 1,3-propanediol is 2.1, 2.9, and 3.1 .ANG., resp. These data indicate that the decay length is inversely proportional to the cube root of the no. of solvent mols. per unit vol. Thus, the decay length of the solvation pressure depends on the packing of the solvent mols. in the interbilayer space but is not strongly dependent on either the solvent's dielec. const. or the dipole moment. The magnitude of the solvation pressure, which is largest in H2O and smallest in 1,3-propanediol, varies with the square of the dipole potential as measured in monolayers in equil. with bilayers.

L8 ANSWER 48 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1989:227443 CAPLUS
DN 110:227443
TI Repulsive interactions between uncharged bilayers. Hydration and fluctuation pressures for monoglycerides
AU ***McIntosh, Thomas J.*** ; Magid, Alan D.; Simon, Sidney A.
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biophys. J. (1989), 55(5), 897-904
CODEN: BIOJAU; ISSN: 0006-3495
DT Journal
LA English
AB Pressure vs. distance relations were obtained for solid (gel) and neat (liq.-cryst.) phase uncharged lipid bilayers by the use of x-ray diffraction anal. of osmotically stressed monoglyceride aq. dispersions and multilayers. For solid phase monoelaidin bilayers, the interbilayer repulsive pressure decays exponentially from a bilayer sepn. of .apprx.7 .ANG. at an applied pressure of 3 .times. 107 dyn/cm2 to a sepn. of .apprx.11 .ANG. at 0 applied pressure, where an excess water phase forms. The decay length is .apprx.1.3 .ANG., which is similar to the value previously measured for gel phase phosphatidylcholine bilayers. This implies that the decay length of the hydration pressure does not depend critically on the presence of zwitterionic head groups in the bilayer surface. For liq.-cryst. monocaprylin, the repulsive pressure vs. distance curve has 2 distinct regions. In the 1st region, for bilayer sepns. of .apprx.3-8 .ANG. and applied pressures of 3 .times. 108 to 4 .times. 106 dyn/cm2, the pressure decays exponentially with a decay length

of .apprx.1.3 .ANG.. In the 2nd region, for bilayer sepns. of .apprx.8-22 .ANG. and applied pressures of 4 .times. 106-1 .times. 105 dyn/cm2, the pressure decays much more gradually and is inversely proportional to the cube of the distance between bilayers. These data imply that 2 repulsive pressures operate between liq.-cryst. monocaprylin bilayers, the hydration pressure, which dominates at small (3-8 .ANG.) bilayer sepns., and the fluctuation pressure, which dominates at larger bilayer sepns. (>8 .ANG.) and strongly influences the hydration properties of the liq.-cryst. bilayers. Thus, due primarily to thermally induced fluctuations, monocaprylin bilayers imbibe considerably more water than do monoelaidin bilayers. For both monoelaidin and monocaprylin, the measured magnitude of the hydration pressure is proportional to the square of the dipole potential.

L8 ANSWER 49 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1989:511310 CAPLUS
DN 111:111310
TI Neutron and x-ray diffraction structural analysis of phosphatidylinositol bilayers
AU McDaniel, Robert V.; ***McIntosh, Thomas J.***
CS Dep. Physiol. Biophys., State Univ. New York, Stony Brook, NY, USA
SO Biochim. Biophys. Acta (1989), 983(2), 241-6
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB Phosphatidylinositol (PI) bilayers, squeezed together by applied osmotic pressures, were studied by both neutron diffraction and x-ray diffraction. The lamellar repeat period for PI bilayers decreased from 9.5 nm at an applied pressure of 1.1 .times. 106 dyn/cm2 (1.1 atm) to 5.4 nm at an applied pressure of 1.6 .times. 107 dyn/cm2 (16 atm). Further increases in applied pressure, up to 2.7 .times. 109 dyn/cm2 (2700 atm) reduced the repeat period by only .apprx.0.3 nm, to 5.1 nm. Thus, a plot of applied pressure vs. repeat period shows a sharp upward break for repeat periods less than .apprx.5.4 nm. For repeat periods of <5.4 nm, anal. of neutron-scattering d. profiles and electron-d. profiles indicates that the structure of the PI bilayers changes as the bilayers are dehydrated, even though there are only small changes in the repeat period. These structural changes are most likely due to removal of water from the headgroup regions of the bilayer. D2O/H2O exchange expts. show that, at an applied pressure of 2.8.107 dyn/cm2, water is located between adjacent PI headgroups in the plane of the bilayer. Thus, although electrostatics provide the dominant long-range repulsive interaction, hydration repulsion and steric hindrance between PI headgroups from apposing bilayers provide the major barriers for the close approach of adjacent PI bilayers for repeat periods <5.4 nm. This structural anal. also indicates that the phosphoinositol group extends from the plane of the bilayer into the fluid space between adjacent bilayers. This extended orientation for the headgroup is consistent with electrophoretic measurements on PI vesicles.

L8 ANSWER 50 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1989:35688 CAPLUS
DN 110:35688
TI Cholesterol modifies the short-range repulsive interactions between phosphatidylcholine membranes

AU ***McIntosh, Thomas J.*** ; Magid, Alan D.; Simon, Sidney A.
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Biochemistry (1989), 28(1), 17-25
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Pressure vs. distance relationships were obtained for egg phosphatidylcholine bilayers contg. a range of cholesterol concns. Water was removed from between adjacent bilayers by the application of osmotic pressures in the range of 0.4-2600 atm (4 .times. 105-2.6 .times. 109 dyn/cm2), and the distance between adjacent bilayers was obtained by Fourier anal. of x-ray diffraction data. For applied pressures up to .apprx.50 atm and bilayer surface sepns. of 15-5 .ANG., the incorporation of up to equimolar cholesterol has little influence on plots of pressure vs. bilayer sepn. However, for the higher applied pressures, cholesterol reduces the interbilayer sepn. distance by an amt. that depends on the cholesterol concn. in the bilayer. For example, the incorporation of equimolar cholesterol reduces the distance between bilayers by .ltoreq.6 .ANG. at an applied pressure of 2600 atm. At this applied pressure, electron d. profiles show that the high-d. head-group peaks from apposing bilayers have merged. This indicates that equimolar concns. of cholesterol spread the lipid mols. apart in the plane of the bilayer enough to allow the phosphatidylcholine head groups from apposing bilayers to interpenetrate as the bilayers are squeezed together. All of these x-ray and pressure-distance data indicate that, by reducing the vol. fraction of phospholipid head groups, cholesterol markedly reduces the steric repulsion between apposing bilayers but has a much smaller effect on the sum of the longer ranged repulsive hydration and fluctuation pressures. Increasing concns. of cholesterol monotonically increase the dipole potential of egg phosphatidylcholine monolayers, from 415 mV with no cholesterol to 493 mV with equimolar cholesterol. These dipole measurements predict that cholesterol should increase slightly the magnitude of the hydration pressure, in qual. agreement with the x-ray results. These observations are pertinent to cholesterol's role in vesicle adhesion and fusion and also imply that cholesterol can alter the membrane binding and permeability of ions and certain drugs and metabolites.

L8 ANSWER 51 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1989:2663 CAPLUS
DN 110:2663
TI Studies of the ethanol-induced interdigitated gel phase in phosphatidylcholines using the fluorophore 1,6-diphenyl-1,3,5-hexatriene
AU Nambi, Parthasarathy; Rowe, Elizabeth S.; ***McIntosh, Thomas J.***
CS Med. Cent., Univ. Kansas, Kansas City, KS, 66100, USA
SO Biochemistry (1988), 27(26), 9175-82
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB The transition of 1,2-dipalmitoylphosphatidylcholine (DPPC) and 1,2-distearoylphosphatidylcholine (DSPC) to the interdigitated phase in the presence of EtOH using the fluorescence properties of the commonly used fluorophore 1,6-diphenyl-1,3,5-hexatriene was detected. By correlating fluorescence and X-ray diffraction results, the use of

fluorescence to study the phase transition from the noninterdigitated to the interdigitated phase was demonstrated. Using this method, the temp. and EtOH concn. dependence of the induction of the interdigitated phase of DSPC and DPPC were investigated; the induction of interdigitation by EtOH is temp. dependent, with higher temp. favoring interdigitation. The temp.-EtOH phase diagrams were detd. for DPPC and DSPC.

L8 ANSWER 52 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1988:637635 CAPLUS
DN 109:237635
TI Magnitude and range of the hydration pressure between lecithin bilayers as a function of headgroup density
AU Simon, Sidney A.; ***McIntosh, Thomas J.*** ; Magid, Alan D.
CS Med. Cent., Duke Univ., Durham, NC, USA
SO J. Colloid Interface Sci. (1988), 126(1), 74-83
CODEN: JCISA5; ISSN: 0021-9797
DT Journal
LA English
AB The hydration repulsive pressure was measured between phosphatidylcholine bilayers as a function of area per lipid mol. by a comparison of x-ray diffraction data from 3 different lipid structures (the gel, liq.-cryst., and interdigitated phases). In the interdigitated phase, the frozen lipid hydrocarbon chains from apposing bilayers fully interpenetrate, and so this phase has nearly twice the interfacial area per zwitterionic headgroup as the gel phase. The magnitude of the hydration pressure significantly decreases with increasing area per mol., but the range of this pressure is nearly independent of the area per mol. These data also indicate that the hydration pressure strongly depends on the dipole potential of the bilayer. This observation suggests a common mechanism for the action of a wide range of membrane fusogens, all of which reduce dipole potential and would therefore be expected to reduce the repulsive hydration pressure between bilayer surfaces.

L8 ANSWER 53 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1986:84051 CAPLUS
DN 104:84051
TI Structure of the crystalline bilayer in the subgel phase of dipalmitoylphosphatidylglycerol
AU Blaurock, Allen E.; ***McIntosh, Thomas J.***
CS Dep. Biochem., Univ. North Carolina, Chapel Hill, NC, 27514, USA
SO Biochemistry (1986), 25(2), 299-305
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB The structure of the subgel phase of dipalmitoylphosphatidylglycerol (DPPG) was analyzed by x-ray diffraction techniques. Diffraction recorded from highly oriented DPPG specimens in the subgel phase extends to 2-.ANG. resoln. There are sharp lamellar reflections on the meridian, and other reflections lie on a series of wide-angle lattice lines parallel to the meridian and crossing the equator in the range 8-2 .ANG.. The wide-angle lattice lines consist of radially sharp reflections centered on the equator of the x-ray film and also a series of broader, off-equatorial max. The lattice lines indicate that the DPPG mols. in each bilayer crystallize in a 2-dimensional oblique lattice with dimensions a = 5.50, b

= 7.96 .ANG., and .gamma. = 100.5.degree.; these oblique lattices are not regularly aligned from bilayer to bilayer. Anal. of the lamellar diffraction shows that the bilayer has about the same thickness in the subgel and gel (L.beta.') phases. In the direction normal to the hydrocarbon chains, the chains are significantly closer together in the subgel phase as compared to the normal L.beta.' gel phase but have about the same sepn. as the chains in polyethylene and the cryst. n-alkanes. The bilayer thickness, area/lipid mol., and intensity distribution along the lattice lines all indicate that in the subgel phase the hydrocarbon chains are tilted 30-35.degree. from the normal to the bilayer plane. In the subgel phase, the lateral packing of chains is much the same as in simple long-chain hydrocarbons such as polyethylene and crystn. n-alkanes, whereas the influence of the DPPG head group causes the chains to tilt relative to the bilayer normal.

L8 ANSWER 54 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1986:564247 CAPLUS
DN 105:164247
TI The influence of anesthetics on the structure and thermal properties of saturated lecithins
AU Simon, Sidney A.; ***McIntosh, Thomas J.*** ; Hines, Michael L.
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Mol. Cell. Mech. Anesth., [Int. Conf.], 3rd (1986), Meeting Date 1984, 297-308. Editor(s): Roth, Sheldon H.; Miller, Keith W. Publisher: Plenum, New York, N. Y.
CODEN: 55EJAB
DT Conference; General Review
LA English
AB A review with 33 refs.

L8 ANSWER 55 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1986:84050 CAPLUS
DN 104:84050
TI A subtransition in a phospholipid with a net charge, dipalmitoylphosphatidylglycerol
AU Wilkinson, D. Allan; ***McIntosh, Thomas J.***
CS Allegheny Singer Res. Inst., Pittsburgh, PA, 15212, USA
SO Biochemistry (1986), 25(2), 295-8
CODEN: BICHAW; ISSN: 0006-2960
DT Journal
LA English
AB Suspensions of dipalmitoylphosphatidylglycerol (DPPG) were analyzed by differential scanning calorimetry, equil. and differential scanning dilatometry, and x-ray diffraction techniques. After the DPPG suspensions are stored several days at 2.degree., a new phase transition is obsd. at a lower temp. than either the main transition or the pretransition. This subtransition has an enthalpy of .apprx.6 kcal/mol and occurs at .apprx.20.degree., the exact temp. depending on the buffer used. The lipid partial specific vol. increases by 0.035 mL/g upon warming through the subtransition. X-ray diffraction patterns from suspensions in the subgel phase contain orders of a lamellar repeat and several addnl. sharp and broad wide-angle reflections at 8-2 .ANG.. As the H2O content in the specimen is reduced, the lamellar repeat period decreases, whereas the spacings and intensities of the addnl. wide-angle reflections are

unchanged. These data indicate that on incubation at 2.degree., the lipid mols. crystallize in the plane of each bilayer. X-ray expts. also show that this subgel phase converts to the normal L.beta.' gel phase above the subtransition.

L8 ANSWER 56 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1986:104726 CAPLUS
DN 104:104726
TI X-ray diffraction studies of the cholera toxin receptor, GM1
AU McDaniel, Robert V.; ***McIntosh, Thomas J.***
CS Health Sci. Cent., State Univ. New York, Stony Brook, NY, 11794, USA
SO Biophys. J. (1986), 49(1), 94-6
CODEN: BIOJAU; ISSN: 0006-3495
DT Journal
LA English
AB X-ray diffraction studies of phosphatidylcholine (PC)-ganglioside GM1 multilamella liposomes showed that the polar head group of GM1 is fully extended over the bilayer surface. The extension is .ltoreq.15 .ANG. from the center of the PC head group or 21 .ANG. from the hydrocarbon-water interface.

L8 ANSWER 57 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1985:433739 CAPLUS
DN 103:33739
TI Observation of an interdigitated gel phase in dipalmitoylphosphatidylglycerol bilayers treated with ionene-6,6
AU Tirrell, David A.; Turek, Anne B.; Wilkinson, D. Allan; ***McIntosh,*** *** Thomas J.***
CS Dep. Polym. Sci. Eng., Univ. Massachusetts, Amherst, MA, 01003, USA
SO Macromolecules (1985), 18(7), 1512-13
CODEN: MAMOBX; ISSN: 0024-9297
DT Journal
LA English
AB X-ray diffraction reveals that adsorption of ionene-6,6 on the surfaces of dipalmitoylphosphatidylglycerol bilayers induces the formation of an unusual gel phase in which the hydrocarbon tails of apposed monolayers are deeply interpenetrated; terminal Me groups of the hydrocarbon chains are thus in contact with the hydrophobic polymethylene spacer. This is the 1st observation of this unusual lipid phase in polymer/lipid mixts.

L8 ANSWER 58 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1986:16753 CAPLUS
DN 104:16753
TI Control of bilayer self-assembly through polymer adsorption
AU Tirrell, David A.; Turek, Anne B.; Wilkinson, D. Allan; ***McIntosh,*** *** Thomas J.***
CS Dep. Polym. Sci. Eng., Univ. Massachusetts, Amherst, MA, 01003, USA
SO Polym. Prepr. (Am. Chem. Soc., Div. Polym. Chem.) (1985), 26(2), 196-7
CODEN: ACPPAY; ISSN: 0032-3934
DT Journal
LA English
AB An interdigitated gel phase of dipalmitoylphosphatidylglycerol (DPPG) and aliph. ionene polymers (ionene-X,Y, where X and Y are the no. of methylene groups in the polymer repeating unit) was prepd. and characterized. Addn.

of ionene-3,3, ionene-6,3, or ionene-6,6 raised the melting temp. of DPPG and eliminated the characteristic pretransition phase. X-ray diffraction studies of DPPG-ionene-6,6 bilayers indicated formation of a lipid phase with hydrocarbon chains that were normal to the bilayer surface and fully interdigitated, in contrast to the L.beta.' phase characteristic of DPPG layers; electron d. patterns across the membrane calcd. from the diffraction patterns confirmed the interdigitation and indicated narrowing of the bilayer thickness. The other 2 ionenes had similar effects.

L8 ANSWER 59 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1983:469835 CAPLUS
DN 99:69835
TI Bilayer induced diastereomeric kinetic differentiation
AU Petter, Russell C.; Mitchell, John C.; Brittain, William J.; ***McIntosh, Thomas J.*** ; Porter, Ned A.
CS Dep. Chem., Duke Univ., Durham, NC, 27706, USA
SO J. Am. Chem. Soc. (1983), 105(17), 5700-1
CODEN: JACSAT; ISSN: 0002-7863
DT Journal
LA English
AB The diastereomeric amphipathic (.pi.)- and meso-R1[RO2C(CH2)4]C(CN)N:NC(CN)[(CH2)4CO2R]R1 (meso-I; R = H, R1 = hexyl) (meso-II) were prepd. and sepd. by reverse phase high-pressure liq. chromatog.; (.+-.)-II is resolved via (-)-quinine. The decompn. rate was detd. in PhCl or multilamellar vesicles of dipalmitoylphosphatidylcholine at 60.degree.. The decompn. rate of meso-II is 6.2 times greater than that of (.+-.)-I in the vesicle and 1.5 times greater in the isotropic PhCl; the decompn. rate of meso-I (R = Me, R1 = hexyl) and (.+-.)-I (R = Me, R1 = hexyl) were the same in PhCl. The conformation of I in the soln. and in the vesicle and the bilayer-induced stereochem. control of chem. reactivity are discussed.

L8 ANSWER 60 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1983:449220 CAPLUS
DN 99:49220
TI A bicontinuous tetrahedral structure in a liquid-crystalline lipid
AU Longley, William; ***McIntosh, Thomas J.***
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Nature (London) (1983), 303(5918), 612-14
CODEN: NATUAS; ISSN: 0028-0836
DT Journal
LA English
AB The x-ray diffraction pattern of glycerol monooleate in the presence of excess water at 22.degree. fits a primitive cubic lattice structure with the material in the crystal arranged in a tetrahedral way. The lipid appears to form a single bilayer, continuous in 3 dimensions, sepg. 2 continuous interlinked networks of water. Each of the water networks has the symmetry of the diamond crystal structure, and the bilayer lies in the space between them following a surface resembling H. A. Schwarz's tetrahedral surface.

L8 ANSWER 61 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1982:610925 CAPLUS
DN 97:210925

TI Morphology of the intermediate stages in the lamellar to hexagonal lipid phase transition
AU Borovyagin, V. L.; Vergara, Juan A.; ***McIntosh, Thomas J.***
CS Inst. Biol. Phys., Puschino, 142292, USSR
SO J. Membr. Biol. (1982), 69(3), 199-212
CODEN: JMBBBO; ISSN: 0022-2631
DT Journal
LA English
AB The addn. of Ca2+ to suspensions of egg phosphatidylcholine and cardiolipin converts multiwalled liposomes to the hexagonal phase. This lamellar-to-hexagonal phase transition was studied by freeze-fracture, thin-section electron microscopy, and x-ray diffraction. The intermediate stages were morphol. characterized. The 1st step in the transition involved the invagination and fusion of bilayers, marked by the appearance of lipidic intramembrane particles and craterlike indentations as the large liposomes are converted to smaller flattened and elongated vesicles. The next step is the formation of tightly packed hexagonal arrays of tubules, each tubule being .apprx.11-15 nm in diam. These tubules are filled with fluid and a lipid bilayer forms the wall of each cylinder. Finally this tubular bilayer phase in converted to the hexagonal phase, where the distance between tubes is 5.5-7.5 nm.

L8 ANSWER 62 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1982:176568 CAPLUS
DN 96:176568
TI Influence of cholesterol on water penetration into bilayers
AU Simon, Sidney A.; ***McIntosh, Thomas J.*** ; Latorre, Ramon
CS Med. Cent., Duke Univ., Durham, NC, 27710, USA
SO Science (Washington, D. C., 1883-) (1982), 216(4541), 65-7
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB X-ray diffraction and capacitance measurements were used to calc. the depth to which water penetrates in fully hydrated bacterial phosphatidylethanolamine bilayers in the presence and absence of cholesterol. The data indicate that cholesterol decreases the depth of water penetration by .apprx.2.5 .ANG..

L8 ANSWER 63 OF 66 USPATFULL
AN 80:26611 USPATFULL
TI Adjustable safety stands for barbell plates
IN ***McIntosh, Thomas J.*** , 910 Edenridge Dr., Youngstown, OH, United States 44512
PI US 4205838 19800603
AI US 1978-907205 19780518 (5)
DT Utility
FS Granted
EXNAM Primary Examiner: Apley, Richard J.
LREP Harpman, Webster B.
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 1 Drawing Page(s)
LN.CNT 95
AB Adjustable safety stands for catching plates of a barbell exercising

device positioned on either side of an exercising bench.

L8 ANSWER 64 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1980:71445 CAPLUS
DN 92:71445
TI The dielectric constant of phospholipid bilayers and the permeability of membranes to ions
AU Dilger, James P.; McLaughlin, Stuart G. A.; ***McIntosh, Thomas J.*** ; Simon, Sidney A.
CS Dep. Physiol. Biophys., State Univ. New York, Stony Brook, NY, 11794, USA
SO Science (Washington, D. C.) (1979), 206(4423), 1196-8
CODEN: SCIEAS; ISSN: 0036-8075
DT Journal
LA English
AB The Born charging equation predicts that the permeability of a phospholipid bilayer membrane to ions should depend markedly on the dielec. const. of the membrane. Increasing the dielec. const. of an artificial bilayer increases its permeability to perchlorate or thiocyanate by a factor of 1000, to a value comparable to that of mitochondrial membranes.

L8 ANSWER 65 OF 66 CAPLUS COPYRIGHT 2001 ACS
AN 1979:2004 CAPLUS
DN 90:2004
TI The effect of cholesterol on the structure of phosphatidylcholine bilayers
AU ***McIntosh, Thomas J.***
CS Dep. Anat., Duke Univ. Sch. Med., Durham, N. C., USA
SO Biochim. Biophys. Acta (1978), 513(1), 43-58
CODEN: BBACAQ; ISSN: 0006-3002
DT Journal
LA English
AB The effect of cholesterol on the structure of phosphatidylcholine bilayers was investigated by x-ray diffraction methods. Electron profiles at 5 .ANG. resoln. along with chain tilt and chain packing parameters were obtained and compared for phosphatidylcholine-cholesterol bilayers and for pure phosphatidylcholine bilayers in both the gel and liq. cryst. states. The cholesterol in the bilayer was localized by noting the position of discrete elevations in the electron d. profiles. Cholesterol can either increase or decrease the width of the bilayer depending on the phys. state and chain length of the lipid before the introduction of cholesterol. For satd. phosphatidylcholines contg. 12-16 carbons/chain, cholesterol increases the width of the bilayer as it removes the chain tilt from gel state lipids or increases the trans conformations of the chains for liq. cryst. lipids. However, cholesterol reduces the width of 18 carbon chain bilayers below the phase transition temp. as the long phospholipid chains must deform or kink to accommodate the significantly shorter cholesterol mol. Although cholesterol has a marked effect on hydrocarbon chain organization, the phosphatidylcholine head group conformation is unchanged by the addn. of cholesterol to the bilayer. The head group is oriented parallel to the plane of the bilayer for phosphatidylcholine in the gel and liq. cryst. states and this orientation is not changed by the addn. of cholesterol.

L8 ANSWER 66 OF 66 CAPLUS COPYRIGHT 2001 ACS

AN 1971:434479 CAPLUS
DN 75:34479
TI Response to warfarin in hypothyroid rats
AU ***McIntosh, Thomas J.*** ; Wilson, William Ralph; Waters, Lysle; Fouts, James R.
CS Coll. Med., Univ. Iowa, Iowa City, Iowa, USA
SO Eur. J. Pharmacol. (1971), 14(2), 176-82
CODEN: EJPHAZ
DT Journal
LA English
AB Prolongation of the 1-stage prothrombin time after a single i.v. dose of warfarin sodium (I) was less at 24 hr in thyroidectomized (Tx) rats than in untreated control animals, but if the prothrombin response was examd. over the duration of its effect, the response of I was significantly greater in the Tx rats; plasma half-life of I was significantly longer in Tx rats. No differences were noted in the calculated vols. of distribution, the plasma protein binding of I, or in the total plasma protein and albumin concns. between Tx and control rats. Thus hypothyroid rats may not be resistant to the anticoagulant effect of I, but actually are more sensitive than are normal rats.

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E1 1 SNYDER DAVID O/AU
E2 6 SNYDER DAVID R/AU
E3 44 --> SNYDER DAVID S/AU
E4 1 SNYDER DAVID SCOTT/AU
E5 1 SNYDER DAVID STEPHEN/AU
E6 3 SNYDER DAVID T/AU
E7 67 SNYDER DAVID W/AU
E8 1 SNYDER DAVID WELLS/AU
E9 1 SNYDER DAYLE O/AU
E10 1 SNYDER DEAN E/AU
E11 2 SNYDER DECEASED DAVID/AU
E12 1 SNYDER DECEASED DAVID B/AU

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L10 36 DUP REM L9 (9 DUPLICATES REMOVED)

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YOU HAVE REQUESTED DATA FROM 36 ANSWERS - CONTINUE? Y/(N):y

L10 ANSWER 1 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:85574 BIOSIS
DN PREV200100085574
TI Solid cancers after bone marrow transplantation.
AU Bhatia, Smita (1); Louie, Andrew D.; Bhatia, Ravi; O'Donnell, Margaret R.; Fung, Henry; Kashyap, Ashwin; Krishnan, Amrita; Molina, Arturo; Nademanee, Auayporn; Niland, Joyce C.; Parker, Pablo A.; ***Snyder, David S.*** ;

Spielberger, Ricardo; Stein, Anthony; Forman, Stephen J.
CS (1) Division of Pediatric Oncology, City of Hope National Medical Center, 1500 E. Duarte Road, Duarte, CA, 91010-3000: sbhatia@smtplink.coh.org USA
SO Journal of Clinical Oncology, (January 15, 2001) Vol. 19, No. 2, pp. 464-471. print.
ISSN: 0732-183X.
DT Article
LA English
SL English
AB Purpose: To evaluate the incidence and associated risk factors of solid cancers after bone marrow transplantation (BMT). Patients and Methods: We analyzed 2,129 patients who had undergone BMT for hematologic malignancies at the City of Hope National Medical Center between 1976 and 1998. A retrospective cohort and nested case-control study design were used to evaluate the role of pretransplantation therapeutic exposures and transplant conditioning regimens. Results: Twenty-nine patients developed solid cancers after BMT, which represents a two-fold increase in risk compared with a comparable normal population. The estimated cumulative probability (+- SE) for development of a solid cancer was 6.1% +- 1.6% at 10 years. The risk was significantly elevated for liver cancer (standardized incidence ratio (SIR), 27.7; 95% confidence interval (CI), 1.9 to 57.3), cancer of the oral cavity (SIR, 17.4; 95% CI, 6.3 to 34.1), and cervical cancer (SIR, 13.3; 95% CI, 3.5 to 29.6). Each of the two patients with liver cancer had a history of chronic hepatitis C infection. All six patients with squamous cell carcinoma of the skin had chronic graft-versus-host disease. The risk was significantly higher for survivors who were younger than 34 years of age at time of BMT (SIR, 5.3; 95% CI, 2.7 to 8.6). Cancers of the thyroid gland, liver, and oral cavity occurred primarily among patients who received total-body irradiation. Conclusion: The risk of radiation-associated solid tumor development after BMT is likely to increase with longer follow-up. This underscores the importance of close monitoring of patients who undergo BMT.

L10 ANSWER 2 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2001:388400 BIOSIS
DN PREV200100388400
TI Myeloperoxidase immunoreactivity in adult acute lymphoblastic leukemia.
AU Arber, Daniel A. (1); ***Snyder, David S.*** ; Fine, Miriam; Dagis, Andrew; Niland, Joyce; Slovak, Marilyn L.
CS (1) Division of Pathology, City of Hope National Medical Center, 1500 E Duarte Rd, Duarte, CA, 91010 USA
SO American Journal of Clinical Pathology, (July, 2001) Vol. 116, No. 1, pp. 25-33. print.
ISSN: 0002-9173.
DT Article
LA English
SL English
AB To evaluate the frequency and significance of myeloperoxidase positivity in adult acute lymphoblastic leukemia (ALL), bone marrow biopsy material from 82 adults with ALL was evaluated with a polyclonal myeloperoxidase (pMPO) antibody. Nineteen cases (23%) demonstrated evidence of pMPO immunoreactivity. Positive cases were precursor B-cell lineage, and CD13 or CD15 expression was more frequent than in the pMPO-negative cases. A subset of pMPO-positive cases studied with a monoclonal MPO antibody was

negative. Western blot analysis using the pMPO antibody showed the expected 55-kd band for myeloperoxidase in pMPO-positive and pMPO-negative ALLs, suggesting a lack of specificity of this antibody in ALL. Forty-two percent (8/19) of the pMPO-positive ALL cases demonstrated evidence of t(9;22) by either karyotype or polymerase chain reaction analysis. The pMPO-positive ALLs had a lower frequency of extramedullary disease than the pMPO-negative group and a trend toward improved overall survival compared with the pMPO-negative group. Immunoreactivity with pMPO in adult ALL may lead to an incorrect interpretation of biphenotypic acute leukemia using a recently described scoring system, and a revision to that scoring system is proposed to accommodate pMPO-positive ALL.

L10 ANSWER 3 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2
AN 2000:158724 BIOSIS
DN PREV200000158724
TI Predictors of therapy-related leukemia and myelodysplasia following autologous transplantation for lymphoma: An assessment of risk factors.
AU Krishnan, Amrita; Bhatia, Smita (1); Slovak, Marilyn L.; Arber, Daniel A.; Niland, Joyce C.; Nademanee, Auayporn; Fung, Henry; Bhatia, Ravi; Kashyap, Ashwin; Molina, Arturo; O'Donnell, Margaret R.; Parker, Pablo A.; Sniecinski, Irena; ***Snyder, David S.*** ; Spielberger, Ricardo; Stein, Anthony; Forman, Stephen J.
CS (1) Division of Pediatric Oncology, City of Hope National Medical Center, 1500 East Duarte Road, Duarte, CA, 91010-3000 USA
SO Blood., (March 1, 2000) Vol. 95, No. 5, pp. 1588-1593. ISSN: 0006-4971.
DT Article
LA English
SL English
AB We analyzed data on 612 patients who had undergone high-dose chemoradiotherapy (HDT) with autologous stem cell rescue for Hodgkin's disease (HD) and non-Hodgkin's lymphoma (NHL) at the City of Hope National Medical Center, to evaluate the incidence of therapy-related myelodysplasia (t-MDS) or therapy-related acute myeloid leukemia (t-AML) and associated risk factors. A retrospective cohort and a nested case-control study design were used to evaluate the role of pretransplant therapeutic exposures and transplant conditioning regimens. Twenty-two patients developed morphologic evidence of t-MDS/t-AML. The estimated cumulative probability of developing morphologic t-MDS/t-AML was 8.6% +- 2.1% at 6 years. Multivariate analysis of the entire cohort revealed stem cell priming with VP-16 (RR = 7.7, P = 0.002) to be independently associated with an increased risk of t-MDS/t-AML. The influence of pretransplant therapy on subsequent t-MDS/t-AML risk was determined by a case-control study. Multivariate analysis revealed an association between pretransplant radiation and the risk of t-MDS/t-AML, but failed to reveal any association with pretransplant chemotherapy or conditioning regimens. However, patients who had been primed with VP-16 for stem cell mobilization were at a 12.3-fold increased risk of developing t-AML with 11q23/21q22 abnormalities (P = 0.006). Patients undergoing HDT with stem cell rescue are at an increased risk of t-MDS/t-AML, especially those receiving priming with VP-16 for peripheral stem cell collection.

L10 ANSWER 4 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2001:330630 BIOSIS

DN PREV200100330630
TI PCR-negative molecular remissions in chronic-, accelerated-, and blast crisis-phase CML patients treated with STI571, an Abl-specific kinase inhibitor.
AU Shah, Neil P. (1); ***Snyder, David S.*** ; Nicoll, John M. (1); McMahon, Ross J.; Hsu, Nicholas C. (1); Forman, Stephen J.; Ford, John M.; Sawyers, Charles L. (1); Paquette, Ronald L. (1)
CS (1) Medicine, Division of Hematology/Oncology, UCLA School of Medicine, Los Angeles, CA USA
SO Blood, (November 16, 2000) Vol. 96, No. 11 Part 1, pp. 471a. print.
Meeting Info.: 42nd Annual Meeting of the American Society of Hematology San Francisco, California, USA December 01-05, 2000 American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English
SL English
AB STI571 is a novel tyrosine kinase inhibitor with relatively specific activity against the Bcr-Abl fusion protein. As previously reported (Druker et al, Amer Soc Hem 3082 (1999) abstract) STI571 has activity in Philadelphia chromosome-positive leukemias. Our institution is participating in large international multicenter studies of STI571 in chronic and advanced stage chronic myelogenous leukemia (CML). In clinical trials, we have observed 20 cases of cytogenetic remission in response to STI571 as monotherapy, as assessed by both karyotype and fluorescence in situ hybridization (FISH). In an effort to determine if minimal residual disease is detectable by the most sensitive molecular methods currently available, we have extracted RNA from leukocytes of patients who have no evidence of the Philadelphia chromosome by FISH. Using a reverse transcriptase polymerase chain reaction (RT-PCR) assay, we have identified six individuals in whom the Bcr-Abl transcript cannot be detected at a sensitivity of 1/105 cells including two patients who were in accelerated phase and one who was in blast crisis at the time therapy was instituted. As an internal control, c-Abl expressed from unrearranged chromosome 9 was detected by RT-PCR in all samples, attesting to the quality of the RNA utilized in this analysis. Furthermore, the fusion Bcr-Abl transcript was detected in all patients tested who had cytogenetic evidence of disease. The ability to assess for molecular remission by RT-PCR may be of great assistance in guiding clinical decisions in cases of complete cytogenetic remission. For patients who have evidence of disease only by RT-PCR, a quantitative assay is currently being used to assess tumor burden. Quantitative RT-PCR will provide the only means of staging disease in this subgroup of patients.

L10 ANSWER 5 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:169838 BIOSIS
DN PREV200000169838
TI Cardioprotection afforded by estrogen on adrenergic nerve terminals in menopause depends on hormonal effectiveness.
AU Eskin, Bernard A. (1); Roberts, Jay (1); ***Snyder, David S. (1)***
CS (1) Medical College of Pennsylvania and Hahnemann University School of Medicine, Philadelphia, PA USA
SO Journal of the American College of Cardiology., (Feb., 2000) Vol. 35, No. 2 suppl. A, pp. 252A.

Meeting Info.: 29th Annual Scientific Session of the American College of Cardiology. Anaheim, California, USA March 12-15, 2000
ISSN: 0735-1097.
DT Conference
LA English
SL English

L10 ANSWER 6 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 3
AN 2000:27525 BIOSIS
DN PREV200000027525
TI Inhibition of bcr-abl oncogene expression by novel deoxyribozymes (DNAzymes.
AU Wu, Yaping; Yu, Lijuan; McMahon, Ross; Rossi, John J.; Forman, Stephen J.; ***Snyder, David S. (1)***
CS (1) Department of Hematology/Bone Marrow Transplantation, City of Hope National Medical Center, 1500 E. Duarte Road, Duarte, CA, 91010 USA
SO Human Gene Therapy, (Nov. 20, 1999) Vol. 10, No. 17, pp. 2847-2857.
ISSN: 1043-0342.
DT Article
LA English
SL English
AB Deoxyribozymes, or DNA enzymes (DNAzymes), are novel nucleic acids that have the ability to bind to specific sequences of RNA, and to cleave the target site catalytically. DNAzymes are smaller and more efficient enzymatically than ribozymes (RZs), which are catalytic nucleic acids synthesized from ribonucleotides. We have designed three DNAzymes that specifically target the two variants of the p210 bcr-abl gene (splice 1, b3a2; splice 2, b2a2) and the p190 variant (e1a2). The cleavage sites for these DNAzymes are located 5 nucleotides (nt) 5' from the fusion site for b3a2, and only 1 nt 5' from the fusion sites for b2a2 and e1a2. We have shown in cell-free in vitro cleavage assays that these DNAzymes efficiently cleave their respective substrates. Mutated DNAzymes, in which only one critical base has been altered, do not cleave these targets. We have used a serum-resistant cytofectin (GS 2888; Gilead) to transfect the DNAzymes into target K562 cells, which express p210bcr-abl. In short-term transfection assays, the DNAzymes specifically inhibited p210bcr-abl protein expression by K562 cells by about 40%, and inhibited cell growth by more than 50% in a 6-day liquid culture assay. We have also transfected freshly isolated CD34+ bone marrow cells from patients with CML with the DNAzymes, which specifically inhibited the growth of bcr-abl-positive CFU-Mix colonies by 53-80%. The potential advantages of anti-bcr-abl DNAzymes over RZs include the following: DNAzymes are much less expensive to synthesize; they are more resistant to serum; and the anti-b2a2 DNAzyme cleaves at a site only 1 nt away from the fusion site, whereas its hammerhead RZ counterpart cleaves this target at a site 8 nt 3' to the fusion site, well within abl exon 2. DNAzymes are novel RNA-cleaving molecules that may significantly improve our ability to inhibit bcr-abl oncogene expression in Ph-positive target cells.

L10 ANSWER 7 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 2000:46940 BIOSIS
DN PREV200000046940
TI Extremely efficient transfection of Philadelphia chromosome-positive leukemia cells utilizing anti-bcr-abl cholesterol-conjugated DNAzymes.

AU ***Snyder, David S. (1)*** ; Swiderski, Piotr (1); McMahon, Ross (1); Yu, Lijuan (1); Li, Ming-Jie (1); Rossi, John J. (1); Forman, Stephen J. (1); Wu, Yaping (1)
CS (1) Hematology/Bone Marrow Transplantation, City of Hope Medical Center, Duarte, CA USA
SO Blood, (Nov. 15, 1999) Vol. 94, No. 10 SUPPL. 1 PART 1, pp. 398a. Meeting Info.: Forty-first Annual Meeting of the American Society of Hematology New Orleans, Louisiana, USA December 3-7, 1999 The American Society of Hematology
. ISSN: 0006-4971.
DT Conference
LA English

L10 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 2000:177321 CAPLUS
DN 132:202825
TI Cyclosporine, methotrexate, and prednisone compared with cyclosporine and prednisone for prevention of acute graft-vs.-host disease: effect on chronic graft-vs.-host disease and long-term survival
AU Ross, Maureen; Schmidt, Gerhard M.; Niland, Joyce C.; Amylon, Michael D.; Dagis, Andrew C.; Long, Gwynn D.; Nademanee, Auayporn P.; Negrin, Robert S.; O'Donnell, Margaret R.; Parker, Pablo M.; Smith, Eileen P.; ***Snyder, David S.*** ; Stein, Anthony S.; Wong, Ruby M.; Forman, Stephen J.; Blume, Karl G.; Chao, Nelson J.
CS Stanford University Medical Center, Stanford, CA, USA
SO Biol. Blood Marrow Transplant. (1999), 5(5), 285-291
CODEN: BBMTF6; ISSN: 1083-8791
PB Carden Jennings Publishing
DT Journal
LA English
AB Graft-vs.-host disease (GVHD) is a major predictor of outcome following allogeneic bone marrow transplantation (BMT). For patients alive at day 100 after BMT, the presence or absence of chronic GVHD is one of the most important determinants of survival and quality of life. We wished to det. the effects on chronic GVHD of two regimens used for the prophylaxis of acute GVHD: cyclosporine, methotrexate, and prednisone (CSA/MTX/PSE) and cyclosporine and prednisone (CSA/PSE). One hundred forty-nine evaluable patients were entered into the acute GVHD study. As of 31 Mar. 1997, 63 mo after the last patient underwent BMT, the median survival time was 4.5 yr (range 0.09-9.9). The incidence of chronic GVHD was independent of the prophylactic regimen (55 vs. 54%), and extensive chronic GVHD occurred in 25 and 24% of patients receiving CSA/MTX/PSE and CSA/PSE, resp. Of note, the median Karnofsky performance status of both groups was 100% (range 70-100%), reflecting the low incidence of extensive chronic GVHD. Survival rates free of chronic GVHD were 52 vs. 42% ($p = 0.29$) for patients receiving CSA/MTX/PSE vs. CSA/PSE. The incidence of relapse was also similar in both groups of patients. These data suggest that the combinations of CSA/MTX/PSE and CSA/PSE result in comparable chronic GVHD-free survival without an increase in leukemic relapse.
RE.CNT 25
RE
(1) Atkinson, K; Blood 1990, V75, P2459 MEDLINE
(2) Chao, N; Biol Blood Marrow Transplant 1996, V2, P86 MEDLINE
(5) Dulude, G; J Exp Med 1999, V189, P1329 CAPLUS

(9) Nesic, D; J Immunol 1998, V160, P3705 CAPLUS
(11) Parker, P; Blood 1995, V86, P3604 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 9 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1998:761797 CAPLUS
DN 130:17217
TI Vaccine against lipopolysaccharide core
IN Bennett-Guerrero, Elliott; Barclay, George Robin; Poxton, Ian Raymond; McIntosh, Thomas James; ***Snyder, David Scott***
PA Medical Defense Technologies, Llc, USA
SO PCT Int. Appl., 51 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9851217	A1	19981119	WO 1998-US9988	19980515
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, GW, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9874912	A1	19981208	AU 1998-74912	19980515
EP 1011440	A1	20000628	EP 1998-922339	19980515
R: BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE				

PRAI US 1997-46680 P 19970516
WO 1998-US9988 W 19980515
AB Complete core LPS (lacking O-polysaccharide side chains) from Gram-neg. bacteria are incorporated into a vaccine typically in liposomes. The complete core of E. coli K 12 is particularly useful. Upon administration to a mammal the vaccine stimulates synthesis of antibodies which are cross-protective against smooth and rough forms of LPS from at least two different Gram-neg. bacterial strains having different core structures.
RE.CNT 9
RE
(1) Dale, P; The Journal of Infectious Diseases 1992, V166, P316 CAPLUS
(2) Dipadova, F; Infection and Immunity 1993, V61(9), P3863 CAPLUS
(3) Fang, I; Infection and Immunity 1993, V61(9), P3873 CAPLUS
(4) Green, S; Advances in Experimental Medicine and Biology 1995, V383, P83 CAPLUS
(6) Poxton, I; Journal of Immunological Methods 1995, V186, P1 CAPLUS
ALL CITATIONS AVAILABLE IN THE RE FORMAT

L10 ANSWER 10 OF 36 USPATFULL
AN 1998:6245 USPATFULL
TI Orifice drain stop
IN Gallagher, Stephen W., Birmingham, MI, United States
Snyder, David S. , Canton, MI, United States
PA Ford Global Technologies, Inc., Dearborn, MI, United States (U.S.

corporation)
PI US 5709309 19980120
AI US 1996-609413 19960301 (8)
RLI Continuation of Ser. No. US 1994-335013, filed on 7 Nov 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Shoap, Allan N.; Assistant Examiner: Hylton, Robin A.
LREP Kelley, David B.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 359
AB A sound attenuating drain stop for an orifice in an automotive floor pan has a resilient plug portion disposed in the orifice and a drainage bore extending axially therethrough, an annular groove for receiving the body panel so as to secure the plug portion thereto, and a compliant element completely obstructing the bore and selectively unobstructing cross-sectional areas of the bore in response to weight variation of fluid thereabove. The compliant element has a resilient, three-legged bridge member spanning the bore and deflectable under the weight of a first predetermined quantity of fluid to drain fluid above the element, and three pie-shaped flexible flaps defined by the bridge member and extending from an interior surface of the bore to the bridge member, the flexible flaps deflectable under the weight of a second predetermined quantity of water when the bridge member is undeflected.

L10 ANSWER 11 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1999:77864 BIOSIS
DN PREV199900077864
TI The immunophenotype of blast transformation of chronic myelogenous leukemia: A high frequency of mixed lineage phenotype in "lymphoid" blasts and a comparison of morphologic, immunophenotypic, and molecular findings.
AU Khalidi, Hasan S.; Brynes, Russell K.; Medeiros, L. Jeffrey; Chang, Karen L.; Slovak, Marilyn L.; ***Snyder, David S.*** ; Arber, Daniel A. (1)
CS (1) Div. Pathology, City Hope National Med. Cent., 1500 East Duarte Road, Duarte, CA 91010 USA
SO Modern Pathology, (Dec., 1998) Vol. 11, No. 12, pp. 1211-1221. ISSN: 0893-3952.
DT Article
LA English
AB Immunophenotypic studies have a limited role in the diagnosis of chronic myelogenous leukemia (CML) but are increasingly being used in CML blast transformation (BT). Determination of the cell lineage of CML blasts is clinically important because patients with lymphoid blast transformation have a better response to chemotherapy and longer survival than those with other lineages. We studied the morphologic, cytochemical, immunophenotypic, cytogenetic, and molecular features of 20 patients with Philadelphia chromosome-positive CML and more than 10% blast cells in peripheral blood or bone marrow. The blasts were morphologically heterogeneous. CD33 was expressed in 19 cases (95%), followed by CD13 (85%), CD11c (80%), CD36 (60%), CD117 (40%), and CD15 (30%). Seven cases (35%) had a precursor-B lymphoid immunophenotype, and 13 (65%) had a predominantly myeloid immunophenotype. Of the former group, of which only

one had a pure lymphoid phenotype, terminal deoxynucleotidyl transferase (TdT) and CD19 were expressed in 100%, CD10 in 85.7%, and CD20 in 14.3%. Of the latter group, all 13 expressed from 3 to 6 myeloid antigens, with 46.2% myeloperoxidase positive and 69.2% CD61 positive. No cases were interpreted as T lineage, but the T-cell antigens CD3, CD4, CD5, and CD7 were expressed in 5.0, 40.0, 5.3 and 30.0% of all cases, respectively. In most cases, the immunophenotype of the CML blasts could not be predicted from their morphologic features. Polymerase chain reaction showed that 80.0% of the lymphoid group and 37.5% of the myeloid group had immunoglobulin heavy-chain gene rearrangements. The frequent lineage infidelity of the blast cells in CML BT seems to be related to the stem cell origin of this disorder. Such lineage infidelity, however, makes classification of many cases difficult and the significance of and criteria for biphenotypic blast crisis of CML is yet to be determined.

L10 ANSWER 12 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 4
AN 1998:8370 BIOSIS
DN PREV199800008370
TI Results of high-dose therapy and autologous bone marrow/stem cell transplantation during remission in poor-risk intermediate- and high-grade lymphoma: International index high and high-intermediate risk group.
AU Nademanee, Auayporn (1); Molina, Arturo; O'Donnell, Margaret R.; Dagis, Andrew; ***Snyder, David S.*** ; Parker, Pablo; Stein, Anthony; Smith, Eileen; Planas, Ina; Kashyap, Ashwin; Spielberger, Ricardo; Fung, Henry; Wong, K. K.; Somlo, George; Margolin, Kim; Chow, Warren; Sniecinski, Irena; Vora, Nayana; Blume, Karl G.; Niland, Joyce; Forman, Stephen J.
CS (1) Dep. Hematol. Bone Marrow Transplantation, City Hope Natl. Med. Cent., 1500 E. Duarte Rd., Duarte, CA 91010 USA
SO Blood, (Nov. 15, 1997) Vol. 90, No. 10, pp. 3844-3852. ISSN: 0006-4971.
DT Article
LA English
AB We have conducted a pilot study to investigate the role of high-dose therapy and autologous bone marrow/stem cell transplantation (ASCT) during first complete or partial remission in 52 patients with poor-risk aggressive lymphoma. There were 42 patients with intermediate-grade or immunoblastic lymphoma who were considered to be high (60%) and high-intermediate risk (40%) groups at diagnosis based on the age-adjusted International Prognostic Index (IPI) and 10 patients with high-grade, SNCCL (small non-cleaved cell, Burkitt's, and non-Burkitt's), who at presentation had poor risk features defined as elevated serum lactate dehydrogenase level, stage IV, and bulky mass gtoreq10 cm. The median age was 34 years (range, 16 to 56 years). Thirty-nine were transplanted in first complete remission and 13 in first partial remission after conventional therapy. Conditioning regimens consisted of total body irradiation (TBI) administered as a single fraction 750 cGy in 3 patients and in fractionated doses for a total of 1,200 cGy in 44 patients, in combination with 60 mg/kg etoposide and 100 mg/kg cyclophosphamide. Five patients with prior radiotherapy received 450 mg/m2 carmustine instead of TBI. Stem cell sources were either bone marrow and/or peripheral blood. No in vitro purging was used. All patients engrafted. Two SNCCL patients died of venoocclusive disease at 25 days and acute leukemia at 27 months posttransplantation. There were six relapses at 1.5 to 12.8 months posttransplantation. At a median followup of 44 months (range, 1 to 113

months), the estimated 3 year overall survival (OS) and disease-free survival (DFS) for all patients was 84% (95% confidence interval (CI), 70% to 92%) and 82% (95% CI, 68% to 91%), respectively. In the subset of patients with intermediate-grade and immunoblastic lymphoma, the 3-year DFS was 89% (95% CI, 74% to 96%) for all patients, 87% (95% CI, 67% to 96%) for high risk patients, and 92% (95 CI, 61 % to 99%) for high-intermediate risk patients. The 3-year OS and DFS for SNCCL patients were identical at 60% (95% CI, 30% to 84%). These results suggest that high-dose therapy and ASCT during first remission may improve the survival and prognosis of patients with poor-risk intermediate- and high-grade lymphoma. A prospective randomized study comparing high-dose therapy and ASCT with conventional chemotherapy in IPI high-risk patients with aggressive non-Hodgkin's lymphoma should be undertaken.

L10 ANSWER 13 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1998:391432 CAPLUS
DN 129:119665
TI Fractionated total-body irradiation, etoposide, and cyclophosphamide followed by allogeneic bone marrow transplantation for patients with high-risk or advanced-stage hematological malignancies
AU Long, Gwynn D.; Amylon, Michael D.; Stockerl-Goldstein, Keith E.; Negrin, Robert S.; Chao, Nelson J.; Hu, Wendy W.; Nademanee, Auayporn P.; ***Snyder, David S.*** ; Hoppe, Richard T.; Vora, Nayana; Wong, Ruby; Niland, Joyce; Reichardt, Volker L.; Forman, Stephen J.; Blume, Karl G.
CS Department of Medicine, Division of Bone Marrow Transplantation, Stanford University Medical Center, Stanford, CA, USA
SO Biol. Blood Marrow Transplant. (1997), 3(6), 324-330
CODEN: BBMTF6; ISSN: 1083-8791
PB Carden Jennings Publishing
DT Journal
LA English
AB Myeloablative therapy followed by allogeneic bone marrow transplantation (BMT) has proven to be curative therapy in patients with hematol. malignancies. Relapse, however, remains a major cause of treatment failure for patients with advanced disease. During the past 15 yr, we have gained considerable experience with the combination of fractionated total-body irradn. (FTBI) and etoposide followed by allogeneic BMT for hematol. malignancies. In an attempt to decrease post-transplant relapse rates, 67 patients under the age of 50 yr with high-risk or advanced-stage hematol. malignancies received an intensified regimen of FTBI and etoposide plus cyclophosphamide followed by BMT from a genotypically-matched related donor. The regimen consisted of 1320 cGy of FTBI in 11 fractions, 60 mg/kg of etoposide (VP-16), and 60 mg/kg of cyclophosphamide (CY). Fifty-three patients received cyclosporine and prednisone for graft-vs.-host disease (GVHD) prophylaxis and 14 patients received cyclosporine, methotrexate, and prednisone. Diagnosis at BMT included 45 patients with acute leukemia, 7 patients with chronic leukemia, and 15 patients with high-grade non-Hodgkin's lymphoma (NHL). Actuarial disease-free survival (DFS) at 3 yr was 42% .+-. 12% for the entire group with a median follow-up of 50 mo (range 20-74) for 28 patients who remain alive in continued complete remission (CR). Actuarial 3-yr-DFS was 38% .+-. 14% in 52 patients with acute or chronic leukemia and 60% .+-. 25% in 15 patients with NHL with relapse rates of 45% .+-. 16% and 21% .+-. 11%, resp. DFS at 3 yr was 40% .+-. 18% in 32 patients

with acute leukemia in 1st relapse or 2nd CR or chronic myelogenous leukemia in accelerated phase, and was 32% .+-. 22% in 20 patients with more advanced disease. Regimen related mortality occurred in 9 patients-4, veno-occlusive disease of the liver; 2, multi-organ failure; 1, diffuse alveolar hemorrhage; 1, central nervous system (CNS) hemorrhage; 1, adult respiratory distress syndrome (ARDS). The combination of FTBI, etoposide, and cyclophosphamide followed by allogeneic BMT is an effective and relatively well-tolerated regimen for patients with advanced hematol. malignancies. The role for this regimen should be further defined by prospective clin. trials.

L10 ANSWER 14 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1998:396425 CAPLUS
DN 129:170159
TI Ribozyme-mediated inhibition of a Philadelphia chromosome-positive acute lymphoblastic leukemia cell line expressing the p190 bcr-abl oncogene
AU ***Snyder, David S.*** ; Wu, Yaping; Mcmahon, Ross; Yu, Lijuan; Rossi, John J.; Forman, Stephen J.
CS Department of Hematology and Bone Marrow Transplantation, City of Hope National Medical Center, Beckman Research Institute, Duarte, CA, 91010, USA
SO Biol. Blood Marrow Transplant. (1997), 3(4), 179-186
CODEN: BBMTF6; ISSN: 1083-8791
PB Carden Jennings Publishing
DT Journal
LA English
AB The bcr-abl oncogene is the mol. counterpart of the Philadelphia chromosome (Ph), which is detected in >95% of patients with chronic myelogenous leukemia (CML) and 20-30% of adults with acute lymphoblastic leukemia (ALL). Leukemic cells from patients with CML express the p210 form of the bcr-abl oncogene, whereas in adult Ph+ ALL approx. 50% of cases express the p190 form of the bcr-abl oncogene, and the other 50% express the same p210 gene as is found in CML. In this study, we have designed hairpin ribozymes (RZs) specific for the p190 form of the bcr-abl oncogene to inhibit the growth of a p190 Ph+ ALL cell line, Sup-B15. The RZs cleave p190 RNA substrate in a cell-free in vitro assay. In the presence of the liposome, DMRIE-C, the RZs are protected from serum mediated catalysis in vitro. Anti-p190 RZs transfected with DMRIE-C as the vector into K562 cells, which express the p210 bcr-abl oncogene, are stable intracellularly for up to 96 h. Up to 33% of the DMRIE-C and RZ mixts. are taken up by Sup-B15 cells cultured in suspension. Expression of the p190 bcr-abl protein product is specifically inhibited as demonstrated by Western blot anal. Cell growth of the Sup-B15 cells is completely inhibited by anti-p190 RZs over four days in culture. Anti-p210 RZs have no significant effect on bcr-abl protein expression or cell growth by Sup-B15 cells. RZs may have a role in purging stem cell populations collected from patients with Ph+ ALL in the context of autologous bone marrow transplantation.

L10 ANSWER 15 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 5
AN 1996:424314 BIOSIS
DN PREV199699155370
TI In vivo purging with high-dose cytarabine followed by high-dose chemoradiotherapy and reinfusion of unpurged bone marrow for adult

myelogenous leukemia in first complete remission.
AU Stein, Anthony S. (1); O'Donnell, Margaret R.; Chai, Akiko; Schmidt, Gerhard M.; Nademanee, Auayporn; Parker, Pablo M.; Smith, Eileen P.; ***Snyder, David S.*** ; Molian, Arturo; Stephan, Daniel E.; Spielberger, Ricardo; Somlo, George; Margolin, Kim A.; Vora, Nayana; Lipsett, Jim; Lee, Jennifer; Niland, Joyce; Forman, Stephan J.
CS (1) Dep. Hematology/Bone Marow Transplantation, City Hope Natl. Med. Center, 1500 E. Duarte Rd., Duarte, CA 91010 USA
SO Journal of Clinical Oncology, (1996) Vol. 14, No. 8, pp. 2206-2216. ISSN: 0732-183X.
DT Article
LA English
AB Purpose: To evaluate in a prospective study the efficacy of autologous bone marrow transplantation (BMT) in adult patients with acute myelogenous leukemia (AML) in first remission, using a single course of high-dose Cytarabine (HD Ara-C) consolidation therapy as in vivo purging. Patients and Methods: Sixty consecutive adult patients with AML in first complete remission (CR) were treated with HD Ara-C consolidation therapy as a method of in vivo purging before marrow collection. High-dose therapy consisted of fractionated total-body irradiation (FTBI) 12 Gy, intravenous etoposide 60 mg/kg, and cyclophosphamide 75 mg/kg, followed by reinfusion of cryopreserved marrow. Results: Sixty patients underwent consolidation treatment with HD Ara-C with the intent to treat with aoutologous BMT. Sixteen patients were unable to proceed to autologous BMT (10 patients relapsed, one died of sepsis, one developed cerebellar toxicity, two had inadequate blood counts, and two refused). Forty-four patients underwent autologous BMT and have a median follow-up time of 37 months (range, 14.7 to 68.7) for patients who are alive with no relapse. The cumulative probability of disease-free survival (DFS) at 24 months in the intent-to-treat group is 49% (95% confidence interval (CI), 37% to 62%) and in those who actually underwent autologous BMT is 61% (95% CI, 46% to 74%). The probability of relapse was 44% (95% CI, 31 % to 58%) and 33% (95% CI, 20% to 49%) for the intent-to-treat and autologous BMT patients, respectively. Conclusion: This approach offers a relatively high DFS rate to adult patients with AML in first CR. The results of this study are similar to those achieved with allogeneic BMT.

L10 ANSWER 16 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 6
AN 1995:553965 BIOSIS
DN PREV199698568265
TI Thalidomide as salvage therapy for chronic graft-versus-host disease.
AU Parker, Pablo M. (1); Chao, Nelson; Nademanee, Auayporn; O'Donnell, Margaret R.; Schmidt, Gerhard M.; ***Snyder, David S.*** ; Stein, Anthony S.; Smith, Eileen P.; Molina, Arturo; Stepan, Daniel E.; Kashyap, Ashwin; Planas, Ina; Spielberger, Ricardo; Somlo, George; Margolin, Kim; Zwingenberger, K.; Wilsman, K.; Negrin, Robert S.; Long, Gwynn D.; Niland, Joyce C.; Blume, Karl G.; Forman, Stephan J.
CS (1) Dep. Hematol. and Bone Marrow Transplantation, City of Hope Natl. Med. Cent., 1500 E. Duarte Road, Duarte, CA 91010 USA
SO Blood, (1995) Vol. 86, No. 9, pp. 3604-3609. ISSN: 0006-4971.
DT Article
LA English
AB Thalidomide has been reported to be an effective agent for treatment of

chronic graft-versus-host disease (CGVHD). To determine the efficacy of this agent in patients with refractory CGVHD a total of 80 patients who failed to respond to prednisone (PSE) or PSE and cyclosporine (CSA) were treated with thalidomide. Sixteen patients (20%) had a sustained response, 9 with a complete remission and 7 with a partial response. Twenty-nine patients (36%) had thalidomide discontinued because of side effects, which included sedation, constipation, neuritis, skin rash, and neutropenia. Side effects were reversible with drug discontinuation except for mild residual neuritis in one case. Rashes and neutropenia have not previously been reported as thalidomide side effects when used for CGVHD treatment. We conclude thalidomide is immunosuppressive and active in the treatment of CGVHD. A high incidence of reversible side effects limited dose intensity and reduced the number of patients who could benefit from treatment.

L10 ANSWER 17 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1996:37962 BIOSIS
DN PREV199698610097
TI Busulfan/cyclophosphamide as conditioning regimen for allogeneic bone marrow transplantation for myelodysplasia.
AU O'Donnell, Margaret R. (1); Long, Gwynn D.; Parker, Pablo M.; Niland, Joyce; Nademanee, Auayporn; Amylon, Michael; Chao, Nelson; Negrin, Robert S.; Schmidt, Gerhard M.; Slovak, Marilyn L.; Smith, Eileen P.; ***Snyder, David S.*** ; Stein, Anthony S.; Traweek, Thomas; Blume, Karl G.; Forman, Stephen J.
CS (1) City of Hope National Med. Center, Dep. Hematol. Bone Marrow Transplantation, 1500 E. Duarte Rd., Duarte, CA 91010 USA
SO Journal of Clinical Oncology, (1995) Vol. 13, No. 12, pp. 2973-2979. ISSN: 0732-183X.
DT Article
LA English
AB Purpose: A non-radiation-containing regimen of busulfan and cyclophosphamide (BU/CY) was evaluated for toxicity, relapse, and long-term survival in patients who received allogeneic bone marrow transplantation (BMT) for myelodysplasia (MDS). Patients and Methods: Thirty-eight patients with MDS, including eight with therapy-related MDS, were prepared for BMT using BU/CY. Results: Fourteen patients remain in first remission 18 to 60 months posttransplant. Five patients relapsed after BMT, and four of these patients died. Eight additional patients died of acute or chronic graft-versus-host disease (GVHD), and 11 died of regimen-related toxicity, primarily systemic mycoses. Overall survival rate at 2 years was 45% (95% confidence interval (CI), 0.30 to 0.61), with a 24% probability of relapse (95% CI, 0.10 to 0.49). Regimen-related toxicity was manifested primarily as hepatic dysfunction in 72% of patients, with 16% developing overt venoocclusive disease (VOD). Conclusion: Non-radiation-containing preparative regimens offer long-term survival in allogeneic BMT for MDS that is comparable to that of radiation-containing regimens, and are useful in patients with therapy-related MDS. Monitoring SU levels may reduce regimen-related mortality and improve survival.

L10 ANSWER 18 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 7
AN 1995:174721 BIOSIS
DN PREV199598189021

TI High-dose chemotherapy with or without total body irradiation followed by autologous bone marrow and/or peripheral blood stem cell transplantation for patients with relapsed and refractory Hodgkin's disease: Results in 85 patients with analysis of prognostic factors.

AU Nademanee, Auayporn (1); O'Donnell, Margaret R.; ***Snyder, David S.*** ; Schmidt, Gerhard M.; Parker, Pablo M.; Stein, Anthony S.; Smith, Eileen P.; Molina, Arturo; Stepan, Daniel E.; Somlo, George; Margolin, Kim A.; Sniecinski, Irena; Dagis, Andrew C.; Niland, Joyce; Pezner, Richard; Forman, Stephen J.

CS (1) Dep. Hematol./Bone Marrow Transplantation, City of Hope National Med. Center, 1500 E. Duarte Rd., Duarte, CA 91010 USA

SO Blood, (1995) Vol. 85, No. 5, pp. 1381-1390.
ISSN: 0006-4971.

DT Article

LA English

AB Eighty-five consecutive patients with relapsed or refractory Hodgkin's disease (HD) underwent high-dose chemotherapy or chemo/radiotherapy followed by autologous bone marrow (ABMT) and/or peripheral blood stem cell (PBSC) transplantation. Two preparative regimens were used. Twenty-two patients (26%) without prior radiation received fractionated total body irradiation (FTBI) 1,200 Gy in combination with high-dose etoposide (VP-16) 60 mg/kg and cyclophosphamide (CTX) 100 mg/kg. Sixty-three patients (74%) with prior radiotherapy received carmustine (BCNU) 450 mg/m-2 instead of FTBI. The median age was 32 years (range, 16 to 56). The median number of prior chemotherapy regimens was three (range, 1 to 7). Forty-three patients (51%) received transplants in first relapse or second complete remission (CR), whereas 33 (39%) received transplants after second or subsequent relapse. All relapsed patients, except one, received conventional salvage chemotherapy and/or radiotherapy in an attempt to reduce tumor bulk before transplant. At the time of analysis in April 1994, fifty-seven patients (67%) are alive, including 44 (52%) in continuous CR, with a median follow-up for the surviving patients of 28 months (range, 7 to 66). Thirty patients (35%) relapsed at a median of 9 months (range, 1 to 43). Eleven patients (13%) died of transplant-related complications including veno-occlusive disease of the liver (VOD) in five, acute and late interstitial pneumonitis in three, graft failure in one, cerebral hemorrhage in one, and therapy-induced myelodysplasia (MDS)/acute leukemia in one patient. At a median follow-up of 25 months (range, 0.6 to 66), the cumulative probability of 2-year overall and disease-free survival (DFS) of all 85 patients is 75% (95% confidence interval (CI) 64% to 84%) and 58% (95% CI 47% to 69%), respectively. Three independent prognostic variables were identified by univariate analysis: number of prior chemotherapy regimens, prior radiotherapy, and extranodal disease at ABMT. Multivariate stepwise Cox regression identified the number of prior chemotherapy regimens as the only significant prognostic factor predicting for both relapse and DFS. There were no significant differences in the outcome of the treatment between the two preparative regimens. Our results confirm that high-dose therapy and ABMT is an effective therapy for patients with relapsed or refractory HD. Earlier transplantation is recommended before the development of drug resistance and end organ damage that results from repeated attempts of salvage therapy.

L10 ANSWER 19 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 8
AN 1995:411552 BIOSIS

DN PREV199598425852

TI The Outcome of Matched Unrelated Donor Bone Marrow Transplantation in Patients With Hematologic Malignancies Using Molecular Typing for Donor Selection and Graft-Versus-Host Disease Prophylaxis Regimen of Cyclosporine, Methotrexate, and Prednisone.

AU Nademanee, Auayporn (1); Schmidt, Gerhard M.; Parker, Pablo; Dagis, Andrew C.; Stein, Anthony; ***Snyder, David S.*** ; O'Donnell, Margaret; Smith, Eileen P.; Stephan, Daniel E.; Molina, Arturo; Wong, K. K.; Margolin, Kim; Somlo, George; Littrell, Barbara; Woo, Doni; Sniecinski, Irena; Niland, Joyce C.; Forman, Stephan J.

CS (1) Dep. Hematol. Bone Marrow Transplantation, City Hope Natl. Med. Cent., 1500 E Duarte Rd., Duarte, CA 91010 USA

SO Blood, (1995) Vol. 86, No. 3, pp. 1228-1234.
ISSN: 0006-4971.

DT Article

LA English

AB Graft-versus-host disease (GVHD) is a major obstacle to successful bone marrow transplantation (BMT) from matched unrelated donor (MUD). Currently available HLA-A, -B, and -DR serologic testing may not be sensitive enough to detect clinically relevant donor/recipient (D/R) nonidentity. Better HLA matching of D/R pairs using molecular typing for class If antigens in combination with intensive GVHD prophylaxis may potentially reduce the incidence of GVHD and lead to an improved outcome of MUD transplantation. Between July 1991 and August 1993, thirty consecutive patients with hematologic malignancies underwent MUD transplantation from donors who were identical for HLA -A, -B, and -DR by serologic typing. Twenty-five D/R pairs were matched for DRB and DQB by molecular typing (restriction fragment-length polymorphism and sequence-specific oligonucleotide probe hybridization analyses), whereas five were allele mismatched at either DRB or DQB. All patients also received GVHD prophylaxis with the combination of cyclosporine (CSA), methotrexate (MTX), and prednisone (PSE). The median age was 35 years (range, 15 to 50). The diagnoses were: chronic myelogenous leukemia (CML) in chronic phase (CP) (16), CML in more than CP (3), acute leukemia in more than first complete remission (CR) (8), acute leukemia in first CR (1), and advanced high-grade lymphoma (2). The preparative regimen consisted of 1,320 cGy fractionated total body irradiation (FTBI) and 60 mg/kg cyclophosphamide (CY) daily for 2 days in 17 good-risk patients (CML/CP and acute leukemia first CR); and 1,320 cGy FTBI in combination with 60 mg/kg etoposide and 20 to 60 mg/kg CY in 13 patients with advanced leukemia and lymphoma. All patients received CSA, PSE, and MTX on days 1, 3, 6 for GVHD prophylaxis, and 10 patients also received day +11 MTX. All patients engrafted except one who died early of regimen-related toxicity. The incidence of grade III or IV acute GVHD was 24% (95% confidence interval (CI), 10% to 44%) and that of extensive chronic GVHD was 65% (95% Cl, 43% to 84%). At a median follow-up of 13.6 months, 57% of the patients are alive in remission with a median Karnofsky performance status of 90%. The cumulative probability of 2-year disease-free survival for all patients was 53% (95% Cl, 33% to 71%); for good-risk patients, 71% (95% Cl, 46% to 87%) and for the poor-risk group, 34% (95% Cl, 13% to 64%). Stepwise logistic regression analysis showed that status at BMT was the only significant prognostic variable associated with severe acute GVHD, whereas donor age greater than 30 predicted for extensive chronic GVHD. These results suggest that the utilization of both serologic and molecular typing for D/R matching with an intensive GVHD

regimen may reduce the incidence of acute GVHD and may potentially improve the outcome of unrelated donor BMT. Further controlled clinical trials are warranted to confirm our results.

L10 ANSWER 20 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1995:378962 BIOSIS
DN PREV199598393262
TI Fractionated total body irradiation and high-dose etoposide as a preparatory regimen for bone marrow transplantation for 99 patients with acute leukemia in first complete remission and 94 patients with chronic myelogenous leukemia in chronic phase.
AU ***Snyder, David S.***
CS Stanford, CA USA
SO Bone Marrow Transplantation, (1995) Vol. 15, No. SUPPL. 1, pp. S212.
Meeting Info.: Fifth Biennial Sandoz-Keystone Symposium on Advances and Controversies in Bone Marrow Transplantation Keystone, Colorado, USA January 23-28, 1994
ISSN: 0268-3369.
DT Conference
LA English

L10 ANSWER 21 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 9
AN 1994:547791 BIOSIS
DN PREV199598007339
TI Marrow transplantation from hepatitis C virus seropositive donors: Transmission rate and clinical course.
AU Shuhart, Margaret C. (1); Myerson, David; Childs, Barrett H.; Fingeroth, Joyce D.; Perry, James J.; ***Snyder, David S.*** ; Spurgeon, Catherine L.; Bevan, Carol A.; McDonald, George B.
CS (1) Gastroenterology Hepatology Section, Fred Hutchinson Cancer Res. Cent., 1124 Columbia Street, Seattle, WA 98104 USA
SO Blood, (1994) Vol. 84, No. 9, pp. 3229-3235.
ISSN: 0006-4971.
DT Article
LA English
AB Bone marrow transplant recipients are at risk for acquiring hepatitis C infection from the donated marrow. Twelve patients who were hepatitis C virus (HCV) RNA-negative pretransplant received marrow from anti-HCV seropositive donors. HCV RNA was present in the sera of seven of these donors. After transplant, serial serum specimens were obtained from all marrow recipients for determination of HCV RNA and aminotransferase levels. All seven recipients of marrow from HCV RNA-positive donors were HCV RNA-positive after marrow infusion; none cleared virus from the serum. All five recipients of marrow from anti-HCV seropositive, HCV RNA-negative donors remained free of HCV RNA in serum up to day 100. Abnormal serum aminotransferases were common in both HCV RNA-negative and HCV RNA-positive marrow recipients. One HCV-infected recipient developed marked elevation in aminotransferases after immunosuppressive drugs were stopped. We conclude that the presence of HCV RNA in the serum of marrow donors is an accurate predictor of HCV infection in marrow recipients. The acute infection was subclinical in all patients. The long-term risk of chronic hepatitis C virus infection in these patients remains to be determined.

L10 ANSWER 22 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:535193 BIOSIS
DN PREV199497548193
TI High-dose therapy followed by autologous peripheral-blood stem-cell transplantation for patients with Hodgkin's disease and Non-Hodgkin's lymphoma using unprimed and granulocyte colony-stimulating factor-mobilized peripheral-blood stem cells.
AU Nademanee, Auayporn (1); Sniecinski, Irena; Schmidt, Gerhard M.; Dagis, Andrew C.; O'Donnell, Margaret R.; ***Snyder, David S.*** ; Parker, Pablo M.; Stein, Anthony S.; Smith, Eileen P.; Molina, Arturo; Stepan, Daniel E.; Somlo, George; Margolin, Kim A.; Woo, Doni; et al.
CS (1) Dep. Hematol./Bone Marrow Transplantation, City Hope National Med. Center, 1500 E. Duarte Rd., Duarte, CA 91010 USA
SO Journal of Clinical Oncology, (1994) Vol. 12, No. 10, pp. 2176-2186. ISSN: 0732-183X.
DT Article
LA English
AB Purpose: To evaluate (1) the effect of granulocyte colony-stimulating factor (G-CSF) on peripheral-blood stem-cell (PBSC) mobilization; (2) the rate of hematopoietic recovery after G-CSF-mobilized PBSC transplantation; and (3) the outcome of high-dose myeloablative therapy and PBSC transplantation in patients with relapsed or refractory lymphoma. Patients and Methods: Ninety-five patients with lymphoma underwent high-dose therapy followed by PBSC transplant in three sequentially treated cohorts of patients in a nonrandomized study. The first 30 patients received nonmobilized PBSCs (unprimed) without G-CSF after transplant, the next 26 patients received PBSC that were mobilized with G-CSF 5 mu-g/kg/d (primed-5) plus G-CSF after transplant, and the last 39 patients received PBSC mobilized by G-CSF 10 mu-g/kg/d (primed-10) plus G-CSF after transplant. The conditioning regimen consisted of fractionated total-body irradiation (FTBI) 12 Gy in combination with etoposide 60 mg/kg and cyclophosphamide 100 mg/kg. Patients with prior radiotherapy received carmustine (BCNU) 450 mg/m-2 instead of FTBI. Results: The use of G-CSF-mobilized PBSCs in combination with G-CSF posttransplant resulted in a significantly accelerated time to recovery of both granulocyte and platelet when compared with the unprimed group. The median number of days to an absolute granulocyte count (ANC) of greater than 0.5 times 10-9/L was 10 days for G-CSF primed versus 20 days for the unprimed (P = .0001). The median days to platelet transfusion independence was 16 and 31 days (P = .0001) for the G-CSF primed and unprimed, respectively. There were also significant reductions in the number of platelet (P = .02) and RBC transfusions (P = .006) for the G-CSF primed. Multivariate analysis of prognostic factors identified CD34+ cell dose as the only additional factor predicting engraftment. Sixty-nine patients are alive at a median follow-up of 15.9 months (range, 7.4 to 63.7). The cumulative probability of 2-year disease-free survival is 59% (95% confidence interval (CI), 36% to 79%) and 39% (95% CI 25% to 55%) for patients with Hodgkin's disease and non-Hodgkin's lymphoma, respectively. Conclusion: The use of G-CSF-mobilized PBSC after high-dose myeloablative therapy resulted in a rapid, complete, and sustained hematopoietic recovery. Disease-free survival over 2 years can be achieved in some patients with relapsed lymphoma after high-dose therapy and PBSC transplantation. However, longer follow-up is required to confirm the curability of this approach.

L10 ANSWER 23 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:452678 BIOSIS
DN PREV199497465678
TI Fractionated total-body irradiation and high-dose etoposide as a preparatory regimen for bone marrow transplantation for 94 patients with chronic myelogenous leukemia in chronic phase.
AU ***Snyder, David S. (1)*** ; Negrin, Robert S.; O'Donnell, Margaret R.; Chao, Nelson J.; Amylon, Michael D.; Long, Gwynn D.; Nademanee, Auayporn P.; Stein, Anthony S.; Parker, Pablo M.; et al.
CS (1) Dep. Hematology/Bone Marrow Transplantation, City of Hope Natl. Med. Center, 1500 E. Duarte Road, Duarte, CA 91010 USA
SO Blood, (1994) Vol. 84, No. 5, pp. 1672-1679.
ISSN: 0006-4971.
DT Article
LA English
AB Ninety-four consecutive patients with chronic myelogenous leukemia in first clinical chronic phase, median age of 34.0 years (range, 6.8 to 52.4 years), with a histocompatible sibling donor, were treated with fractionated total body irradiation (1,320 cGy) and high-dose etoposide (60 mg/kg) followed by allogeneic bone marrow transplantation (BMT). The median time from diagnosis to BMT was 7.0 months (range, 2.3 to 72.0 months). Sixty patients were treated before BMT with hydroxyurea alone, four patients with busulfan alone, one patient with interferon alone, and the other 29 patients were treated with various combinations of these drugs. Cumulative probabilities of overall survival, event-free survival, and relapse at 5 years were 73%, 640/o, and 14%, respectively. The median follow-up time for surviving patients was 38 months, ranging from 12 to 88 months. By stepwise Cox regression analysis, significant prognostic variables were age at transplant, acute graft-versus-host disease gtoreq grade II, cytomegalovirus-associated interstitial pneumonitis, and years from diagnosis to BMT.

L10 ANSWER 24 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:360776 BIOSIS
DN PREV199497373776
TI Detection of the Philadelphia chromosome in paraffin-embedded tissue by fluorescence in situ hybridization.
AU Brynes, Russell K. (1); McCourty, Althea; Ho, Jennifer Pelkey; Traweek, S. Thomas; ***Snyder, David S.*** ; Slovak, Marilyn I.
CS (1) Dep. Clin. Pathol., City Hope Natl. Med. Cent., 1500 E. Duarte Road, Duarte, CA 91010 USA
SO Modern Pathology, (1994) Vol. 7, No. 5, pp. 565-569.
ISSN: 0893-3952.
DT Article
LA English
AB The bcr-abl fusion gene situated on the Philadelphia chromosome is a tumor-specific marker for chronic myelogenous leukemia. We evaluated the usefulness of two color fluorescence in situ hybridization with bcr and abl probes as a means of detecting the Philadelphia chromosome in formalin-fixed, paraffin-embedded sections of spleen and lymph node specimens from eight patients with myeloproliferative diseases showing clinical and morphological features of chronic myelogenous leukemia in accelerated phase. Our analysis showed co-localized hybridization signals corresponding to the bcr-abl fusion product in tissue sections from six

patients previously found to have the Philadelphia chromosome by conventional cytogenetics and polymerase chain reaction. The two remaining specimens lacked bcr-abl fusion signals and were obtained from patients who were negative for the Philadelphia chromosome by cytogenetic and polymerase chain reaction analysis. We conclude that fluorescence in situ hybridization is a sensitive method for the detection of the bcr-abl fusion gene in histological specimens from patients with chronic myelogenous leukemia. The technique may become a useful tool in the evaluation of tissue specimens from patients with chronic myelogenous leukemia and related Philadelphia chromosome-positive hematologic malignancies.

L10 ANSWER 25 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1993:205231 CAPLUS
DN 118:205231
TI Ribozyme inhibition of bcr-abl gene expression
IN ***Snyder, David S.*** ; Rossi, John J.; Forman, Stephen J.
PA City of Hope, USA
SO PCT Int. Appl., 30 pp.
CODEN: PIXXD2
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI WO 9303141	A1	19930218	WO 1991-US5443	19910801
W: AU, CA, JP, US				
RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LU, NL, SE				
CA 2092571	AA	19930202	CA 1991-2092571	19910801
AU 9184981	A1	19930302	AU 1991-84981	19910801
EP 551294	A1	19930721	EP 1991-915940	19910801
R: DE, FR, GB				
JP 06501610	T2	19940224	JP 1991-514649	19910801
PRAI WO 1991-US5443		19910801		

AB A method for purging leukemia cells from bone marrow of patients affected with chronic myelogenous leukemia (CML) or acute lymphoblastic leukemia comprises treating the bone marrow with a ribozyme which cleaves mRNA of the bcr-abl gene. A plasmid encoding a hammerhead ribozyme active against the splice 1 mRNA of the bcr-abl gene was prepd. EM-2 cells (derived from a CML patient) were transformed with this plasmid. Inhibition of bcr-abl gene mRNA prodn. and 3H-thymidine incorporation were obsd.

L10 ANSWER 26 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1994:21275 BIOSIS
DN PREV199497034275
TI Fractionated total body irradiation and high-dose etoposide as a preparatory regimen for bone marrow transplantation for 99 patients with acute leukemia in first complete remission.
AU ***Snyder, David S. (1)*** ; Chao, Nelson J.; Amylon, Michael D.; Taguchi, Julie; Long, Gwynn D.; Negrin, Robert S.; Nademanee, Auayporn P.; O'Donnell, Margaret R.; Schmidt, Gerhard M.; et al.
CS (1) Dep. Hematol./Bone Marrow Transplantation, City Hope Natl. Med. Cent., 1500 E. Duarte Road, Duarte, CA 91010 USA
SO Blood, (1993) Vol. 82, No. 9, pp. 2920-2928.

ISSN: 0006-4971.
DT Article
LA English
AB Ninety-nine consecutive patients with acute leukemia in first complete remission under age 50 (median age 27 years; age range 1 to 47 years) with a histocompatible sibling donor were treated with fractionated total body irradiation (1,320 cGy) and high-dose etoposide (60 mg/kg) followed by allogeneic bone marrow transplantation, Sixty-one patients were diagnosed with acute myelogenous leukemia (AML), 34 patients with acute lymphoblastic leukemia (ALL), 3 patients with biphenotypic acute leukemia, and 1 patient with acute undifferentiated leukemia. Thirty of the 34 patients with ALL had at least one of the following high-risk factors: age greater than 30, white blood cell count at presentation gt 25,000/mu-L, extramedullary disease, certain chromosomal translocations, or the need for greater than 4 weeks of induction chemotherapy to achieve first complete remission. Cumulative probabilities of disease-free survival and relapse at 3 years were 61% and 12%, respectively, for the 61 patients with AM L and 64% and 12%, respectively, for the 34 patients with ALL. By stepwise Cox regression analysis, significant prognostic variables for patients with acute myelogenous leukemia were the presence of acute graft-versus-host disease and increasing age, whereas for patients with acute lymphoblastic leukemia, significant variables were age and the development of cytomegalovirus-associated interstitial pneumonia. Complications related to graft-versus-host disease and relapse of leukemia were the major causes of death.

L10 ANSWER 27 OF 36 BIOSIS COPYRIGHT 2001 BIOSIS
AN 1993:408901 BIOSIS
DN PREV199396074626
TI Ribozyme-mediated inhibition of bcr-abl gene expression in a Philadelphia chromosome-positive cell line.
AU ***Snyder, David S. (1)*** ; Wu, Yaping; Wang, Juinn L.; Rossi, John J.; Swiderski, Piotr; Kaplan, Bruce E.; Forman, Stephen J.
CS (1) Dep. Hematol/Bone Marrow Transplantation, City Hope Natl. Med. Cent., 1500 E Duarte Rd, Duarte, CA 91010-0269 USA
SO Blood, (1993) Vol. 82, No. 2, pp. 600-605.
ISSN: 0006-4971.
DT Article
LA English
AB The bcr-abl fusion gene is the molecular counterpart of the Philadelphia chromosome (Ph-1) and is directly involved in the pathogenesis of Ph-1+ leukemia. Inhibition of bcr-abl gene expression may have profound effects on the cell biology of Ph-1+ cells, as recent experiments with antisense oligonucleotides have shown. In this study we have designed and synthesized a unique ribozyme that is directed against bcr-abl mRNA. The ribozyme cleaved bcr-abl mRNA in a cell-free in vitro system. A DNA-RNA hybrid ribozyme was then incorporated into a liposome vector and transfected into EM-2 cells, a cell line derived from a patient with blast crisis of chronic myelogenous leukemia. The ribozyme decreased levels of detectable bcr-abl mRNA in these cells, inhibited expression of the bcr-abl gene product, p210-bcr-abl, and inhibited cell growth. This anti-bcr-abl ribozyme may be a useful tool to study the cell biology of Ph-1+ leukemia and may ultimately have therapeutic potential in treating patients with Ph-1 leukemias.

L10 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1990:585352 CAPLUS
DN 113:185352
TI Human serum and plasma have different sources of epidermal growth factor
AU Lev-Ran, Arye; Hwang, David L.; ***Snyder, David S.***
CS Dep. Diabetes, Endocrinol., Metab., City of Hope Natl. Med. Cent., Duarte, CA, 91010, USA
SO Am. J. Physiol. (1990), 259(3, Pt. 2), R545-R548
CODEN: AJPHAP; ISSN: 0002-9513
DT Journal
LA English
AB EGF was detd. by RIA in serum, plasma, and urine of patients undergoing ablative therapy followed by bone marrow transplantation. The difference between the serum and plasma values reflected the amt. of EGF released from the platelets at the time of blood coagulation. Platelet-derived EGF strongly correlated with platelet count, and the intercept of the regression line was very close to zero; one platelet contained .apprx.2.5 .times. 10-18 g EGF. Correspondingly, when the platelet count dropped after bone marrow ablation from 222 to 33 .times. 109/L, the serum EGF decreased from 603 to 65 pg/mL. Plasma EGF content did not correlate with the platelet count and did not change after bone marrow ablation (before and after the ablation, correspondingly, 290 and 332 pg/mL). HPLC fractionation of serum and plasma showed different mol. mass distribution of EGF-immunoreactive fractions. The main mol. mass components of the plasma EGF did not change after bone marrow ablation. Urine excretion remained unchanged (320 and 314 pmol EGF/mmol creatinine). Whereas platelets are the source of serum EGF, the origin of plasma EGF is different and the search of its origin is warranted.

L10 ANSWER 29 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1989:453505 CAPLUS
DN 111:53505
TI Detection by enzymic amplification of bcr-abl mRNA in peripheral blood and bone marrow cells of patients with chronic myelogenous leukemia
AU Lange, Winand; ***Snyder, David S.*** ; Castro, Rosario; Rossi, John J.; Blume, Karl G.
CS Sch. Med., Stanford Univ., Stanford, CA, USA
SO Blood (1989), 73(6), 1735-41
CODEN: BLOOAW; ISSN: 0006-4971
DT Journal
LA English
AB The Philadelphia chromosome of chronic myelogenous leukemia (CML) patients is caused by a translocation of the c-abl gene from chromosome 9 to the breakpoint cluster region (bcr) on chromosome 22. A new bcr-abl mRNA is expressed in these cases. A modified polymerase chain reaction (PCR) was developed for the detection of this mRNA. The method is extremely sensitive, reliable, and relatively fast. The anal. of peripheral blood or bone marrow cells from CML patients treated with chemotherapy shows that the two possible mRNAs are expressed in various combinations. Even after myeloablative therapy for bone marrow transplantation bcr-abl mRNAs are still expressed. Further studies, however, are necessary to det. the clin. relevance of a small no. of persisting cells expressing the bcr-abl mRNA.

L10 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1989:88118 CAPLUS
DN 110:88118
TI Antiproliferative effects of lipoxygenase inhibitors on malignant human hematopoietic cell lines
AU ***Snyder, David S.*** ; Castro, Rosario; Desforges, Jane F.
CS City of Hope Natl. Med. Cent., Duarte, CA, USA
SO Exp. Hematol. (N. Y.) (1989), 17(1), 6-9
CODEN: EXHMA6; ISSN: 0301-472X
DT Journal
LA English
AB The role of lipoxygenase metabolites in regulating the proliferation of several malignant hematopoietic cell lines, including K562 and EM-2 (chronic myelogenous leukemia blasts), HL-60 (promyelocytic leukemia cells), and U937 (malignant histiocytes) is discussed. Piriprost, a specific inhibitor of 5-lipoxygenase, inhibited proliferation of these cell lines .ltoreq.95%, with 50% cell inhibition at .apprx.3 .times. 10-5M. Other less specific lipoxygenase inhibitors such as caffeic acid, nordihydroguaiaretic acid, and BW755C had similar activity in a [3H]thymidine incorporation assay. In contrast, indomethacin, which is a cyclooxygenase inhibitor, had no suppressive effect in these assays. Inhibition by these drugs was completely reversible. Several nonhematopoietic malignant cell lines were not affected by these drugs. Two specific lipoxygenase metabolites, leukotrine B4 and leukotriene D4, stimulated leukemia cell line proliferation to 150% of control levels when added directly to cell cultures. Thus, certain lipoxygenase products, perhaps leukotrienes, are crit. for the proliferation of malignant hematopoietic cells in vitro. The potential use of lipoxygenase inhibitors as antileukemia agents is discussed.

L10 ANSWER 31 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1987:590556 CAPLUS
DN 107:190556
TI Inhibition of human monocyte antigen presentation, but not HLA-DR expression, by cyclosporine
AU ***Snyder, David S.*** ; Wright, Christine L.; Ting, Carol
CS Dep. Hematol. Bone Marrow Transplant., City of Hope Natl. Med. Cent., Duarte, CA, 91010, USA
SO Transplantation (1987), 44(3), 407-11
CODEN: TRPLAU; ISSN: 0041-1337
DT Journal
LA English
AB The effects of cyclosporine (CsA) on antigen-dependent human T cell proliferation have been studied using tetanus toxoid as the antigen. CsA inhibited antigen-dependent T cell proliferation at concns. as low as 0.1 .mu.g/mL. Preexposure of sepd. monocytes to CsA during the period of antigen processing led to a marked inhibition of proliferation of T cells added subsequently to the monocytes. Monocyte HLA-DR expression, interleukin 1 (IL-1) prodn., and prostaglandin (PG) secretion were not affected by CsA. In particular, human monocyte HLA-DR expression was not inhibited by CsA, even at 10 .mu.g/mL. The addn. of exogenous IL-1 or indomethacin did not reverse the inhibitory effects of CsA. Thus, CsA inhibits antigen-dependent human T cell proliferation, at least in part,

by acting directly on human monocytes to inhibit antigen presentation. The mechanism of action seems to be independent of IL-1 prodn., PG secretion, and HLA-DR expression.

L10 ANSWER 32 OF 36 USPATFULL
AN 86:19120 USPATFULL
TI Paperback display rack
IN Mt. Pleasant, Gregory G., Baldwinsville, NY, United States
Dokoupil, James R., Liverpool, NY, United States
Snyder, David S. , Liverpool, NY, United States
PA Gaylord Bros., Inc., Liverpool, NY, United States (U.S. corporation)
PI US 283279 19860408
AI US 1983-537559 19830930 (6)
PTERM 14 Years
DT Design
FS Granted
EXNAM Primary Examiner: Vales, Carmen H.
LREP Staas & Halsey
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 21

L10 ANSWER 33 OF 36 USPATFULL
AN 86:19113 USPATFULL
TI Periodical display rack
IN Mt. Pleasant, Gregory G., Baldwinsville, NY, United States
Dokoupil, James R., Liverpool, NY, United States
Snyder, David S. , Liverpool, NY, United States
PA Gaylord Bros., Inc., Liverpool, NY, United States (U.S. corporation)
PI US 283272 19860408
AI US 1983-537568 19830930 (6)
PTERM 14 Years
DT Design
FS Granted
EXNAM Primary Examiner: Vales, Carmen H.
LREP Staas & Halsey
CLMN Number of Claims: 1
ECL Exemplary Claim: 1
DRWN 9 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 19

L10 ANSWER 34 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1986:422261 CAPLUS
DN 105:22261
TI Lipoxygenase metabolites of arachidonic acid modulate hematopoiesis
AU ***Snyder, David S.*** ; Desforges, Jane F.
CS Dep. Med., Tufts-New England Med. Cent., Boston, MA, 02111, USA
SO Blood (1986), 67(6), 1675-9
CODEN: BLOOAW; ISSN: 0006-4971
DT Journal
LA English
AB The role of lipoxygenase (LPO) metabolites of arachidonic acid in controlling myelopoiesis and erythropoiesis was studied in vitro.

Monocyte depleted cells (MDC) prepd. from human whole blood or whole mononuclear cells from human bone marrow were cultured in methylcellulose in the presence of various growth factors. Conditioned media contg. human colony-stimulating factors or the tumor-promoting phorbol ester PMA were added to induce myelopoiesis. Semipurified human erythropoietin was added along with an endogenous source of burst-promoting activity to induce erythropoiesis. The LPO inhibitor BW 755C blocked all types of colony formation in a dose-dependent manner, with an ID50 of 20 .mu.g/mL and 5 .mu.g/mL for myeloid and erythroid colonies, resp. MDC depleted of T cells were similarly inhibited by BW 755C. Similar results were seen with 2 other LPO inhibitors, 1-phenyl-3-pyrazolidone, and butylated hydroxyanisole. A 4th LPO inhibitor, nordihydroguaiaretic acid, inhibited at higher concns. Indomethacin, at concns. that inhibit cyclooxygenase, had no significant effect, either alone or in combination with the LPO inhibitors. Thus, certain LPO products may be important mediators of both colony-stimulating factor- and PMA-induced myelopoiesis and of burst-promoting activity/erythropoietin-induced erythropoiesis.

L10 ANSWER 35 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1983:11664 CAPLUS
DN 98:11664
TI Corticosteroids inhibit murine macrophage Ia expression and interleukin 1 production
AU ***Snyder, David S.*** ; Unanue, Emil R.
CS Dep. Pathol., Harvard Med. Sch., Boston, MA, 02115, USA
SO J. Immunol. (1982), 129(5), 1803-5
CODEN: JOIMA3; ISSN: 0022-1767
DT Journal
LA English
AB hydrocortisone (I) [50-23-7] and prednisolone [50-24-8] inhibited macrophage Ia expression, prodn. of interleukin 1, and in accordance with these results, the presentation of antigen for T-cell proliferation. Lymphokine-induced Ia expression was inhibited both at the cellular level in vitro and at the population level in vivo by therapeutic doses (2-5 .times. 10-8M) of both drugs. The results may explain one mechanism by which corticosteroids suppress the induction of the immune response.

L10 ANSWER 36 OF 36 CAPLUS COPYRIGHT 2001 ACS
AN 1983:47604 CAPLUS
DN 98:47604
TI Prostaglandins modulate macrophage Ia expression
AU ***Snyder, David S.*** ; Beller, David I.; Unanue, Emil R.
CS Dep. Pathol., Harvard Med. Sch., Boston, MA, 02115, USA
SO Nature (London) (1982), 299(5879), 163-5
CODEN: NATUAS; ISSN: 0028-0836
DT Journal
LA English
AB Lymphokine-induced I-region-assocd. antigen (Ia) expression by mouse macrophage cells was markedly inhibited by PGE1 [745-65-3] and PGE2 [363-24-6] in a dose-dependent manner, with 50% inhibition at 1.5 .times. 10-10 and 8.6 .times. 10-10M resp. In vivo, i.p. injection of prostaglandins E (50 .mu.g), inhibited the lymphokine-induced development of peritoneal exudates rich in Ia-pos. macrophages. Injection of indomethacin (50 .mu.g) augmented the response to lymphokines and

increased the basal no. of Ia-pos. macrophages. thromboxane B2 [54397-85-2] (10-11-10-8M) was a potent antagonist to the effects of macrophages in vitro. The regulation of Ia expression by prostaglandins could be an important control mechanism in the inductive phase of immune responses.

=> s lipopolysaccharide? or LPS
L11 219032 LIPOPOLYSACCHARIDE? OR LPS

=> s l11 and (complete core)
L12 212 L11 AND (COMPLETE CORE)

=> s l12 and rough
L13 125 L12 AND ROUGH

=> s l13 and (rough complete core)
L14 1 L13 AND (ROUGH COMPLETE CORE)

=> d bib ab

L14 ANSWER 1 OF 1 USPATFULL
AN 1999:4392 USPATFULL
TI Monoclonal antibody against ***LPS*** core
IN Gram, Hermann, Weil-Haltingen, Germany, Federal Republic of
Di Padova, Franco, Birsfelden, Switzerland
Barclay, George Robin, Midlothian, United Kingdom
Poxton, Ian Raymond, Midlothian, United Kingdom
PA Common Services Agency, United States (non-U.S. corporation)
PI US 5858728 19990112
AI US 1996-647144 19960509 (8)
RLI Continuation of Ser. No. US 1993-119046, filed on 30 Sep 1993, now abandoned
PRAI GB 1991-5292 19910313
DT Utility
FS Granted
EXNAM Primary Examiner: Loring, Susan A.
LREP Bell Seltzer Intellectual Property Law Group of Alston & Bird LLP
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 12 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 2426
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides monoclonal antibodies (Mabs) which are cross-protective against endotoxemia caused by at least two different Gram-negative bacterial strains having different core structures; and methods of production of these antibodies. By use of the Kohler/Milstein procedure involving immunization of mice with a number of different ***rough*** strains of heat-killed Gram-negative bacteria, followed by fusion and proper screening of the resulting hybridomas, such murine MAbs are obtained. The murine MAbs may be chimerized or humanized by known methods. For example, a chimeric MAb of IgG isotype is provided in which the hypervariable regions of the heavy chain have the amino acid sequences: Asp Tyr Tyr Met Thr; Leu Ile Arg Asn Lys Arg Asn Gly Asp Thr

Ala Glu Tyr Ser Ala Ser Val Lys; and Gln Gly Arg Gly Tyr Thr Leu Asp Tyr; the hypervariable regions of the light chain have the amino acid sequences: Arg Ala Ser Gln Asn Ile Asn Ile Trp Leu Ser; Lys Ala Ser Asn Leu His Thr; and Leu Gln Gly Gln Ser Tyr Pro Arg Thr; the framework regions in the variable domains are murine and the constant domains are human.

=> d kwic

L14 ANSWER 1 OF 1 USPATFULL
TI Monoclonal antibody against ***LPS*** core
AB . . . of production of these antibodies. By use of the Kohler/Milstein procedure involving immunization of mice with a number of different ***rough*** strains of heat-killed Gram-negative bacteria, followed by fusion and proper screening of the resulting hybridomas, such murine MAbs are obtained.. . .
SUMM . . . prevention, diagnosis and treatment of infectious diseases caused by Gram-negative bacteria and more particularly provides monoclonal antibodies (MAbs) against the ***lipopolysaccharide*** (***LPS*** ; also called endotoxin) constituent of the gram-negative bacterial membranes.
SUMM . . . aeruginosa. Proteus. Enterobacter and Serratia. All Gram-negative bacteria are characterized by a specific type of outer membrane which comprises a ***lipopolysaccharide*** (***LPS***) as major constituent. ***LPS*** plays an essential immunologic and physiopathologic role in the infections and is the major causative agent of septic shock.
SUMM Although the ***LPS*** constituent varies from one species to another, it may be generally described with reference to FIG. 1 as consisting of. . . region (also called O-specific side chain) is highly variable and is composed of repeated oligosaccharide units characteristic of the species. ***LPS*** molecules on the surface of a single cell do not have a constant amount of oligosaccharide units.
SUMM . . . smooth aspect. This is the reason why wild type bacteria are usually referred to as smooth bacteria in contrast with ***rough*** mutants which lack the O-specific side chain and, sometimes, part of the core region and the cultures of which show a ***rough*** aspect. The different types of ***rough*** mutants from Salmonella are conventionally designated by the terms Ra, Rb, Rc, Rd and Re. As seen from FIG. 1, the ***LPS*** of all of them comprises the lipid A structure while the Ra mutant is characterised by a ***complete*** ***core*** region, the Rb mutant is characterised by the absence of N-acetyl-D-glucosamine residue, the Rc mutant is characterised by the absence. . .
SUMM Since treatments for the toxic effect of ***LPS*** are not available. attention has been focused on immunologic methods as an alternative or additional treatment to antibiotic therapy to. . . bacteria, for example, by enhancing opsonization and phagocytosis of the bacterial cells or by neutralization of the biological activity of ***LPS*** . However, the effectiveness of the antisera greatly varies depending upon a large number of factors including, for example, the composition. . .
SUMM . . . may be described as horizontal and vertical. By vertical

cross-reactivity is meant that the MAb reacts with essentially all smooth ***LPS*** molecules of a particular bacterial strain, independent of the length of the O-specific side-chain. By horizontal cross-reactivity is meant that the MAb reacts with ***LPS*** having different core structures. This is necessary because therapy must be started as soon as the bacteremia has been empirically. . .

SUMM Such MAbs must recognize antigenic determinants located in the ***LPS*** structure which is shared by most enterobacteria i.e. Lipid A and the core region. They may be obtained by the. . . & Milstein method which, in particular comprises conventionally immunizing mice with an immunogen in which the inner antigenic epitopes of ***LPS*** are immediately available for raising antibodies. Suitable immunogens include heat-killed ***rough*** mutants of an enterobacterium e.g. the J5 strain of E. coli. Purified ***LPS*** is less suitable as an immunogen.

SUMM . . . fail to be protective against infections. MAbs have often been described as reactive on the basis of binding experiments involving ***rough*** rather than smooth ***LPS*** , and the lack of protectivity of these MAbs may be due to the fact that, in wild-type smooth ***LPS*** , the epitope for which the antibody is specific is not available, being hindered by the core region or the O-specific side chain. In particular, MAbs recognizing epitopes in the Lipid A part of the ***LPS*** molecule are generally ineffective.

SUMM It has now been found that monoclonal antibodies recognizing epitopes in the core region of the ***LPS*** molecule and having both vertical and horizontal cross-reactivity and also cross-protectivity can be obtained by modified and improved immunization and. . .

SUMM Accordingly the present invention provides a monoclonal antibody which recognizes an epitope in the core region of the ***LPS*** molecule and which is cross-protective against endotoxemia caused by at least two different Gram-negative bacterial strains having different core structures.

SUMM . . . an epitope which is already present in the Rc core structure of E. coli and is also present in the ***complete*** ***core*** .

SUMM In E. coli, the MAb of the invention preferably reacts with all common smooth strain isolates, and preferably also with ***rough*** strain mutants of all five core types (R1, R2, R3, R4, and K12). Preferably the MAb is also reactive with. . .

SUMM In contrast to the immunization protocols described in the prior art, in which generally a single type of ***LPS*** (normally as heat-killed bacteria bearing the specific type of ***LPS***) is used as immunogen, MAbs of the present invention may be produced by an immunization protocoll in which the animal to be immunized is exposed to a plurality of types of ***LPS*** molecule. This may be done either by immunization with a cocktail of different ***LPS*** types physically mixed together, or by immunizing in sequence by individual different ***LPS*** types. In both cases it is prefered to use heat-killed bacteria rather than purified ***LPS*** molecules. Other possible immunogens include bacteria killed by means other than heat (e.g. by formaldehyde) and ***LPS*** molecules linked to protein carriers.

SUMM In a first preferred method, mice are immunized with a single cocktail of different strains of heat-killed bacteria, preferably ***rough*** strains having a ***complete*** ***core*** , for example a

mixture of R1, R2, R3 and R4 strains of Ra E. coli. Alternatively two or more such. . . and Salmonella minnesota R60 may be followed a week later by a mixture of E. coli R1, R4 and 018 ***rough*** strain, and then the two injections repeated at further weekly intervals.

SUMM In a second preferred method, mice are immunized sequentially with a number of different ***rough*** strains of heat-killed bacteria, only one strain being administered at any one time. For example mice may be immunized with Pseudomonas PAC 605 ***rough*** mutant followed by E. coli R1, R2 and R3 at monthly intervals.

SUMM . . . cell fusion to make hybridomas by the conventional Kohler-Milstein technique. The booster immunization is preferably by a cocktail of different ***rough*** strain E. coli, even if the primary immunization was carried out by the second preferred method (sequential administration).

SUMM . . . to prior art methods, an initial screening is preferably carried out using a series of mixtures of different smooth and ***rough*** ***LPS*** types to select those MAbs reacting with a wide range of ***LPS*** molecules. In this way, widely cross-reactive MAbs can already be identified at the initial screening stage. For example, each hybridoma supernatant may be screened by testing for reactivity in the ELISA assay with seven different ***LPS*** cocktails and a control, according to the following scheme:

SUMM 3) ***Rough*** ***complete*** ***core*** : EcR1+R4

SUMM 4) ***Rough*** ***complete*** ***core*** : EcR2+EcR3+EcK12+Sm R60

SUMM Inhibition of ***LPS*** -induced IL-6 secretion by murine peritoneal macrophages

SUMM . . . sepsis and its accompanying endotoxemia. These monokines are secreted by macrophages, both in vitro and in vivo, in response to ***LPS*** . A protective anti- ***LPS*** antibody blocks the macrophage stimulation as shown in the following assay:

SUMM . . . Vol. II, Acad. Press (1981):263) and cultured for 4 hrs at 37.degree. C. (i) in the presence or absence of ***LPS*** e.g. ***LPS*** from E. coli R1 (0.05 ng/ml); E. coli R2 (0.05 ng/ml); E. coli R3 (0.05 ng/ml) and E. coli R4. . .

SUMM For the purposes of this patent specification, a MAb is regarded as being protective against a given ***LPS*** if it gives in the above assay a reduction of IL-6 secretion of at least 50% when tested at a concentration of 5 .mu.g/ml, the concentration of purified ***LPS*** being 0.05 ng/ml for ***rough*** ***LPS*** and correspondingly higher for the less active smooth types. A MAb is cross-protective if it is protective against at least two ***LPS*** having different core structures. Preferred cross-protective MAbs are cross-protective against ***LPS*** from different bacterial genera.

SUMM By the use of the above immunization and screening methods, a number of novel mouse anti- ***LPS*** antibodies have been found which cross-react with several ***LPS*** of different genera and exhibit substantial cross-protective activity and that it is possible to construct other ***LPS*** binding molecules derived from these monoclonal antibodies and having the same characteristics since they share regions which determine the binding. . .

SUMM In view of the foregoing, the invention provides a ***LPS*** binding molecule which comprises at least one antigen binding site comprising at least one domain which comprises in sequence, the. . .

SUMM In a first aspect of the invention, the ***LPS*** binding molecule comprises an antigen binding site comprising a single domain.

SUMM In a second aspect of the invention, the ***LPS*** binding molecule comprises at least one antigen binding site comprising:

SUMM By " ***LPS*** binding molecule" is meant any molecule capable of binding to ***LPS*** . The binding reaction may be shown by standard methods (qualitative assays) such as an ELISA using purified ***LPS*** or heat treated bacteria or a Western blotting using purified ***LPS*** ; with reference to a negative control test in which an antigen of unrelated origin, e.g. bovine serum albumin (BSA), is. . .

SUMM 1. Detection of binding to purified ***LPS*** in an ELISA

SUMM Microtitre plates (flat bottomed; microtest III flexible assay plates: Becton Dickinson, Falcon 3912) are coated with purified ***LPS*** at 2 .mu.g/ml in coating buffer (diethylenebarbituric acid-Na salt 30 mM. Na acetate 30 mM, NaCl 116 mM; pH 4.5). 50 .mu.l aliquots of the ***LPS*** solution are distributed into each well. Unrelated protein (BSA, 2% in PBS pH 7.2/0.02% sodium azide) is used to determine. . .

SUMM Advantageously, the purified ***LPS*** which is used is selected from smooth, ***complete*** ***core*** , Rb or Rc ***LPS*** . Examples of smooth ***LPS*** are ***LPS*** extracted from E. coli 0111B4 (Difco), E. coli 0127B8 (Difco), E. coli 0128B12 (Difco), Salmonella typhimurium BO ag 0:4, 5, 12 (SH 4809) (Bio-carb). Suitable ***complete*** ***core*** ***LPS*** , Rb ***LPS*** and Rc ***LPS*** are respectively obtained from S. Minnesota (List) and S. typhimurium SL 684 (Sigma).

SUMM . . . show in tabular form the binding of antibodies WN1 222-5, WN1 58-9, H1 61-2 and SZ27 19.16.07 respectively to purified ***LPS*** from different strains of Gram-negative bacteria.

SUMM Precoated plates are prepared as described in 1. above, using heat killed bacteria (0.5.times.10.sup.8 cells/ml) rather than purified ***LPS*** . The binding reaction is tested and detected as described in 1. above.

SUMM Advantageously, the bacteria are smooth wild type bacteria or ***rough*** Ra, Rb or Rc mutants.

SUMM The bacteria listed in Tables II and III are mostly common clinical isolates. The bacteria and/or the corresponding ***LPS*** are commercially available or are available on request from Dr. I. Poxton, Dept. of Bacteriology, University of Edinburgh, Scotland, or. . .

SUMM 3. Detection of binding to ***LPS*** using Western blotting

SUMM 10 .mu.l aliquots of a ***LPS*** solution at 1 mg/ml are mixed with an equal volume of 0.1M Tris-HCl buffer, pH 6.8 containing 1% (wt/vol) sodium. . .

SUMM In this assay, the antibodies of the invention show a binding reaction with ***LPS*** extracted either from smooth bacteria or from ***rough*** mutants. Particular experiments involving WN1 222-5, WN1 58-9, H1 61-2 and SZ27 19.16.07 are to be seen in FIGS. 4A; 4B, 4C and 4D respectively. The ***LPS*** content extracted from a smooth bacterium is separated by electrophoresis into bands corresponding to ***LPS*** molecules having different molecular weights, depending on the size of the O-specific side chain. These ***LPS*** molecules range from ***LPS*** molecules without any O-specific side chain to ***LPS*** molecules having 40 or more units in the side chain. The antibodies of the invention react with ***rough*** repeating units and all these ***LPS*** molecules, containing O-side chain repeating

units. This indicates that the epitope for which the ***LPS*** -binding molecules of the invention are specific is not hindered by the O-specific side chain. Therefore the majority of ***LPS*** molecules of a smooth bacterium are able to react with an ***LPS*** -binding molecule of the invention.

SUMM Accordingly, the invention also provides an ***LPS*** binding molecule which comprises at least one antigen binding site comprising either a domain having an amino acid sequence substantially. . .

SUMM In view of the foregoing, a more preferred ***LPS*** binding molecule of the invention is selected from a chimeric anti- ***LPS*** antibody which comprises at least

SUMM Alternatively, a ***LPS*** binding molecule of the invention may be selected from a single chain binding molecule which comprises an antigen binding site. . .

SUMM . . . original protein which has substantially identical properties. Thus, by the term "direct equivalents thereof" is meant either any single domain ***LPS*** binding molecule (molecule X)

SUMM (ii) which is capable of binding to ***LPS*** substantially to the same extent as a reference molecule having framework regions identical to those of molecule amino acid 67. . . positions 31-35, 50-67, and 101-109 respectively) identical to those shown in SEQ ID NO:2 or SEQ ID NO:4 or any ***LPS*** binding molecule having at least two domains per binding site (molecule X')

SUMM (ii) which is capable of binding to ***LPS*** substantially to the same extent as a reference molecule having framework regions and constant parts identical to molecule X' but. . .

SUMM One ***LPS*** binding molecule may be considered as binding to ***LPS*** substantially to the same extent as another if the two molecules can be shown effectively to compete with each other in competitive ELISA binding assays on different ***LPS*** molecules, for example on the ***LPS*** from E. coli J5 and from Salmonella Ra 60 and if the binding affinities of the two molecules vary from. . .

SUMM Most preferably, the chimeric anti- ***LPS*** antibody comprises at least

SUMM Conjugates of the ***LPS*** binding molecules of the invention. e.g. enzyme or toxin conjugates, are also included within the scope of the invention, as are ***LPS*** binding molecules labelled with radioactive isotopes or fluorescent markers.

SUMM A ***LPS*** binding molecule of the invention may be produced by recombinant DNA techniques. In view of this, one or more DNA. . .

SUMM (i) DNA molecules encoding a single domain ***LPS*** binding molecule of the invention, a single chain ***LPS*** binding molecule of the invention, a heavy or light chain or fragment thereof of a ***LPS*** binding molecule of the invention and

SUMM (ii) the use of the DNA molecules of the invention for the production of a ***LPS*** binding molecule of the invention by recombinant means.

SUMM In a particular embodiment of the invention, the recombinant means for the production of a ***LPS*** binding molecule includes first and second DNA constructs as described below:

SUMM In another aspect of the invention, there is provided a process for producing a multi-chain ***LPS*** binding molecule which comprises (i) culturing an organism which has been transformed with the first and second DNA constructs of the invention and (ii) recovering an active ***LPS*** binding molecule from the culture.

SUMM (iii) reconstituting in vitro an active ***LPS*** binding molecule from the heavy chain or fragment thereof obtained in (i) and the light chain or fragment thereof obtained. . .

SUMM In a similar manner, there is also provided a process for producing a single chain or single domain ***LPS*** binding molecule which comprises (i) culturing an organism which is transformed with a DNA construct respectively encoding a single chain or single domain ***LPS*** binding molecule of the invention and (ii) recovering said molecule from the culture.

SUMM ***LPS*** binding molecules of the invention exhibit very good protective activity against ***LPS*** of Gram-negative endotoxemia as shown both in the in vitro IL-6 assay described above, and in the following in vivo. . .

SUMM Rabbits are then injected in a marginal ear vein with the ***LPS*** -binding molecule followed 30 min to 2 hr later by ***LPS*** in the same ear vein. ***LPS*** from different E. coli and salmonella, e.g. Salmonella abortus equi may be used. The suitable dose of ***LPS*** -binding molecule is to be determined, depending upon the type of molecule. For example WN1 222-5 is administered at 1 mg. . . mg per kg body weight. For injection, this antibody is also prepared at 1 mg/ml in pyrogen-free saline and the ***LPS*** is injected at 10-100 ng/kg body weight, depending on the ***LPS*** used.

SUMM Control animals receive either ***LPS*** alone or the antibody alone. Rabbits are monitored at 15 min. intervals for a period starting from the injection and. . .

SUMM In this assay, ***LPS*** binding molecules of the invention significantly reduce the increase of temperature in comparison with the negative control (***LPS*** alone). Depending upon the type of ***LPS*** , the % of inhibition may reach levels well above 50%. A protective MAb may be defined in terms of this in vivo assay as one which gives at least 30% inhibition of fever 240 min after an ***LPS*** challenge of 10-100 ng/kg With an antibody dose of 1-5 mg/kg.

SUMM (i) the use of an ***LPS*** binding molecule of the invention for preventing or treating gram-negative endotoxemia in humans

SUMM (ii) a method of preventing or treating gram-negative endotoxemia in humans which comprises administering an effective amount of an ***LPS*** binding molecule of the invention to a patient in need of such treatment.

SUMM (iii) a pharmaceutical composition for preventing or treating Gram-negative bacterial infections in humans which comprises an ***LPS*** binding molecule of the invention and a pharmaceutically acceptable carrier or diluent.

SUMM ***LPS*** binding molecules of the invention, either unlabelled or, preferably, labelled with a radioactive isotope or a fluorescent marker, may also. . . diagnostic purposes to determine the nature, location and extent of Gram-negative bacterial infections, or analytically to detect the presence of ***LPS*** or Gram-negative bacterial contamination in water, foodstuffs, biological fluids, etc. Thus for example a labelled ***LPS*** binding molecule of the invention may be useful for the imaging of localised infectious foci for surgical removal or other treatment. The ***LPS*** binding molecules of the invention may also be attached to a solid phase support-material to form the solid phase of an affinity chromatography purification system for

the removal of ***LPS*** molecules from biological fluids, e.g. blood serum.

DRWD FIG. 1 shows the detailed structure of a Salmonella ***LPS*** molecule, indicating the various Ra-Re ***rough*** mutant types. In this Figure, Abe=abequose, Ac=acetyl, Ara=4-amino-4-deoxy-L-arabinose. Etn=ethanolamine, FA=hydroxy fatty acid, Gal=D-galactose, Glc=D-glucose, GlcN=D-glucosamine, GlcNAc=N-acetyl-d-glucosamine, Hep=heptose, KDO=2-keto-3-deoxyoctonic acid, Man=mannose,. . .

DRWD FIG. 4A shows the binding capacity of monoclonal antibody WN1 222-5 against different ***LPS*** molecules derived from eight different E. coli strains as determined by Western blotting. The drawing represents the spots of the. . .

DRWD FIG. 4B shows the binding capacity of WN1 58-9 against different ***LPS*** molecules derived from eight different bacterial strains as determined by Western blotting. The drawing represents the spots of the gel.. . .

DRWD FIG. 4C shows the binding capacity of H1 61-2 against different ***LPS*** molecules derived from eight different bacterial strains as determined by Western blotting. The drawing represents the spots of the gel.. . .

DRWD FIG. 4D shows the binding capacity of SZ27 19.16.07 against different ***LPS*** molecules derived from eight different bacterial strains as determined by Western blotting. The drawing represents the spots of the gel.. . .

DETD week 2 EcR1+EcR4+Ec018 ***rough*** strain

DETD week 4 EcR1+EcR4+Ec018 ***rough*** strain

DETD . . . PAI-O cell line, using standard procedures. Supernatant from wells containing growing hybridomas were screened using cocktails of different smooth and ***rough*** ***LPS*** as described above, and hybridomas producing cross-reactive MAb's were cloned.

DETD Primary screening was carried out using the following cocktails of different ***rough*** ***LPS*** :

DETD 1) ***complete*** ***core*** : EcR2, EcR3, EcK12

DETD 2) ***complete*** ***core*** : EcR1, EcR4, SmR60

DETD A group of 5 mice received identical immunizations. Antibody responses were monitored in tail bleed samples to purified ***LPS*** antigen from the following strains:

DETD Primary screening was carried out using two ***LPS*** cocktails:

DETD . . . strong responses to both cocktails were selected for further growth. These were then given a secondary screening on 11 different ***LPS*** antigens before selection for cloning. These were:

DETD TABLE IIA

CHEMOTYPE		WN1 222-5
mAb	STRAIN	SUPPLIER
		100 ng/ml
		10 ng/ml
		1 ng/ml
LPS	Smooth	
E. coli		
02		Univ. Edinburgh
		+++++
		++++ ++

LPS Smooth
E. coli
04 Univ. Edinburgh
+++++
+++++
++++

LPS Smooth
E. coli
06 Univ. Edinburgh
+++++
+++++
+++

LPS Smooth
E. coli
012 Univ. Edinburgh
+++++
+++++
++

LPS Smooth
E. coli
015 Univ. Edinburgh
+++++
+++++
++++

LPS Smooth
E. coli
016 Univ. Edinburgh
+++++
+++++
++

LPS Smooth
E. coli
018K- Univ. Edinburgh
+++++
+++++
+++

LPS Smooth
E. coli
018K+ Univ. Edinburgh
+++++
+++++
++++

LPS Smooth
E. coli
026B6 Difco +++++
+++++
+++

LPS Smooth
E. coli
055B5 Difco +++++
++ +

LPS Smooth
E. coli
075 Univ. Edinburgh

+++++
+++++
+++

LPS Smooth
E. coli
086 Univ. Edinburgh
+++++
+++++
+++

LPS Smooth
E. coli
0111B4 Difco +++++
+++++
++

LPS Smooth
E. coli
0127B8 Difco +++++
+++++
+++

LPS Smooth
E. coli
0128B12 Difco ++++ +++ ++

LPS Smooth
E. coli
K235 List +++++
+++++
+++

LPS Smooth
S. minnesota
wt List +++++
+++++
+++

LPS Smooth
S. typhimurium
wt Difco +++++
+++++
++

LPS Smooth
S. typhimurium
B0 ag 0:4,5,12 (SH 4809)
Bio-Carb
+++++
++++ +

LPS Smooth
S. typhimurium
B0 ag 0:1,4,5,12 (SL 3622)
Bio-Carb
+++++
++++ +

LPS Smooth
S. typhimurium
B0 ag 0:4,5,12 2 (SH 4305)
Bio-Carb
++++++

+++++
+

LPS Smooth
S. typhi
D0 ag 0:9,12 Bio-CarbTy)
+++++
+++++
+++

LPS Smooth
S. newport
C2 ag 0:6,8 Bio-Carb
+++++
+++++
+++

LPS Smooth
S. enteridis
D0 ag 0:9,12 (SH 1262)
Bio-Carb
+++++
+++++
+++

LPS Smooth
S. thompson
C1 ag 0:6,7, (ls40)
Bio-Carb
+++++
+++++
++++

LPS Smooth
S. abortus equi
(H1178) Institut Borsiel
+++++
+++++
++++

LPS cCore
E. coli
K12 Univ. Edinburgh
+++++
+++++
++

LPS cCore
E. coli
C62 Univ. Edinburgh
++++ +++++
++

LPS cCore
E. coli
R1 Institut Borstel
+++++
+++++
++

LPS cCore
E. coli
R2 Institut Borstel

+++++
+++++
++

LPS cCore
E. coli
R3 Institut Borstel
+++++
+++++
++++

LPS cCore
E. coli
R4 Institut Borstel
+++++
+++++
+++

LPS cCore
S. minnesota
Ra R60 List +++++
+++++
+++

LPS cCore
S. typhimurium
TV119 Sigma +++++
+++++
+++

LPS cCore
S. typhimurium
1542 Univ. Edinburgh
+++++
+++++
++++

LPS cCore
K. aerogenes
M10B Univ. Edinburgh
- - -

LPS Rb2 S. minnesota
R345 List ++++++
+++++
++++

LPS Rb3 S. minnesota Bio-Carb
++++++
+++++
++

LPS Rc E. coli
J5 List ++++++
+++++
++++

LPS Rc S. typhimurium
878 Univ. Edinburgh
++++++
+++++
++

LPS Rc S. typhimurium
SL684 Sigma ++++++

+++++
++++

LPS Rc P. aeruginosa
PAC605 Univ. Edinburgh
+ + +

LPS RcP-
S. minnesota
R5 List ++++++
+++++
++++

LPS Rd2 E. coli
F583 Sigma ++++++
+++++
+++

LPS Rd1P-
S. minnesota
R7 List +++ ++ +

LPS Rd2 S. minnesota
R4 (V594) Institut Borstel
++++ +++ ++

LPS Re E. coli
K12 (D31m4) List ++++ ++++ ++

LPS Re E. coli
F515 Institut Borstel
+++++
+++++
++++

LPS Re S. minnesota
R595 List + + -

LPS Re S. typhimurium
SL1102 Univ. Edinburgh
- - -

LPS Re S. typhimurium
SL1181 Sigma - - -

Lipid A E. coli
K12 (ex-D31m4)
List - - -

Lipid A S. minnesota
R595 List - - -

BSA - - -

Purified native ***LPS*** (2 ug/ml) were used to coat the plates
Values are reported as O.D., one + equals 0.5 O.D. (405 nm).

DETD TABLE IIB

WN1 58-9 MAb
CHEMOTYPE STRAIN SUPPLIER
100 ng/ml
10 ng/ml
1 ng/ml

LPS Smooth
E. coli
02 Univ. Edinburgh

++++ ++++ +

LPS Smooth
E. coli
04 Univ. Edinburgh
+++++
++++ +

LPS Smooth
E. coli
06 Univ. Edinburgh
++++ +++++
-

LPS Smooth
E. coli
012 Univ. Edinburgh
++++ +++++
+

LPS Smooth
E. coli
015 Univ. Edinburgh
+++++
+++++
· ++

LPS Smooth
E. coli
016 Univ. Edinburgh
++++ +++++
+

LPS Smooth
E. coli
018K- Univ. Edinburgh
++++ ++++ +

LPS Smooth
E. coli
018K+ Univ. Edinburgh
+++++
+++++
++

LPS Smooth
E. coli
026B6 Difco +++++
+++++
+

LPS Smooth
E. coli
055B5 Difco +++ + -

LPS Smooth
E. coli
075 Univ. Edinburgh
++++ ++ -

LPS Smooth
E. coli
086 Univ. Edinburgh
++++ ++++ +

LPS Smooth

E. coli
0111B4 Difco ++++ ++++ +
LPS Smooth
E. coli
0127B8 Difco ++++ +++ +
LPS Smooth
E. coli
0128B12 Difco ++ ++ -
LPS Smooth
E. coli
K235 List ++++ ++++ +
LPS Smooth
S. minnesota
wt List ++++ ++++ +
LPS Smooth
S. typhimurium
wt Difco ++++ ++++ +
LPS Smooth
S. typhimurium
B0 ag 0:4,5,12 (SH 4809)
Bio-Carb
++++ +++ -
LPS Smooth
S. typhimurium
B0 ag 0:1,4,5,12 (SL 3622)
Bio-Carb
++++ +++ +
LPS Smooth
S. typhimurium
B0 ag 0:4,5,12 2 (SH 4305)
Bio-Carb
++++ ++++ +
LPS Smooth
S. typhi
D0 ag 0:9,12 Bio-CarbTy)
+++++
+++++
+
LPS Smooth
S. newport
C2 ag 0:6,8 Bio-Carb
+++++
+++++
+
LPS Smooth
S. enteridis
D0 ag 0:9,12 (SH 1262)
Bio-Carb
+++++
++++ +
LPS Smooth
S. thompson
C1 ag 0:6,7, (ls40)
Bio-Carb

+++++
+++++
++

LPS Smooth
S. abortus equi
(H1178) Institut Borsiel
+++++
+++++
++

LPS cCore
E. coli
K12 Univ. Edinburgh
++++ ++++ +

LPS cCore
E. coli
C62 Univ. Edinburgh
+++++
+++++
+++

LPS cCore
E. coli
R1 Institut Borstel
+++++
+++++
+

LPS cCore
E. coli
R2 Institut Borstel
++++ +++ +

LPS cCore
E. coli
R3 Institut Borstel
+++++
+++++
+

LPS cCore
E. coli
R4 Institut Borstel
++++ +++++
+

LPS cCore
S. minnesota
Ra R60 List ++++ +++++
+

LPS cCore
S. typhimurium
TV119 Sigma ++++ ++++ +

LPS cCore
S. typhimurium
1542 Univ. Edinburgh
++++ +++++
+

LPS cCore
K. aerogenes

M10B Univ. Edinburgh
- - -
LPS Rb2 S. minnesota
R345 List +++++
+++++
+++
LPS Rb3 S. minnesota Bio-Carb
+++++
+++++
+
LPS Rc E. coli
J5 List +++++
+++++
+
LPS Rc S. typhimurium
878 Univ. Edinburgh
+++++
+++++
+
LPS Rc S. typhimurium
SL684 Sigma +++++
+++++
++
LPS Rc P. aeruginosa
PAC605 Univ. Edinburgh
+ + -
LPS RcP.sup.--
S. minnesota
R5 List +++++
+++++
++
LPS Rd2 E. coli
F583 Sigma +++++
+++++
++
LPS Rd1P.sup.--
S. minnesota
R7 List ++++ ++ -
LPS Rd2 S. minnesota
R4 (V594) Institut Borstel
++++ +++ -
LPS Re E. coli
K12 (D31m4) List +++++
+++++
++
LPS Re E. coli
F515 Institut Borstel
+++++
+++++
+++
LPS Re S. minnesota
R595 List + - -
LPS Re S. typhimurium
SL1102 Univ. Edinburgh

- - -

LPS Re S. typhimurium
SL1181 Sigma - - -

Lipid A E. coli
K12 (ex-D31m4)
List - - -

Lipid A S. minnesota
R595 List - - -

BSA - - -

Purified native ***LPS*** (2 .mu.g/ml) were used to coat the plates
Values are reported as O.D., one + equals 0.5 O.D. (405 nm).

. . .

DETD TABLE IIC

HI 61-2 IgG1

CHEMOTYPE	STRAIN	SUPPLIER
	1 .mu.g/ml	
	100 ng/ml	
	10 ng/ml	
	1 ng/ml	

LPS Smooth
E. coli
02 Univ. Edinburgh
++++ +++++
++ -

LPS Smooth
E. coli
06 Univ. Edinburgh
+++ +++++
++ -

LPS Smooth
E. coli
012 Univ. Edinburgh
+++++
+++++
+++++
+++

LPS Smooth
E. coli
015 Univ. Edinburgh
+++++
+++++
++++ +

LPS Smooth
E. coli
016 Univ. Edinburgh
+ ++ - -

LPS Smooth
E. coli
018K- Univ. Edinburgh
+++++
+++++

+++++
+

LPS Smooth
E. coli
018K+ Univ. Edinburgh
+++++
+++++
+++++
++

LPS Smooth
E. coli
026B6 Difco +++++
+++++
+++++
+

LPS Smooth
E. coli
055B5 Difco +++ ++++ - -

LPS Smooth
E. coli
075 Univ. Edinburgh
+++ +++++
+++ -

LPS Smooth
E. coli
086 Univ. Edinburgh
+++++
+++++
++++ +

LPS Smooth
E. coli
0111B4 Difco +++++
+++++
+++++
++

LPS Smooth
E. coli
0127B8 Difco +++++
+++++
+++++
+++

LPS Smooth
E. coli
0128B12 Difco - - - -

LPS Smooth
E. coli
K235 List ++++ +++++
+++ -

LPS Smooth
S. minnesota
wt List ++++ ++++ ++ -

LPS Smooth
S. typhimurium
wt Difco +++++

+++++
+++++
+

LPS cCore
E. coli
K12 Univ. Edinburgh
+++++
+++++
+++++
+++

LPS cCore
E. coli
C62 Univ. Edinburgh
++++++
+++++
+++++
++

LPS cCore
E. coli
R1 Institut Borstel
++++++
+++++
+++++
+++

LPS cCore
E. coli
R2 Institut Borstel
+++++
+++++
+++++
++++

LPS cCore
E. coli
R3 Institut Borstel
+++++
+++++
+++++
++

LPS cCore
E. coli
R4 Institut Borstel
++++++
+++++
+++++
++++

LPS cCore
S. minnesota
Ra R60 List ++++++
+++++
+++++
++++

LPS cCore
S. typhimurium
TV119 Sigma ++++++

+++++
+++++
+

LPS cCore
S. typhimurium
1542 Univ. Edinburgh
+++++
+++++
+++++
++

LPS cCore
K. aerogenes
M10B Univ. Edinburgh
- - - -

LPS Rb2 S. minnesota
R345 List ++++++
+++++
++ -

LPS Rc E. coli
J5 List ++++++
+++++
+++++
++++

LPS Rc S. typhimurium
878 Univ. Edinburgh
++++++
++++++
+++++
++++

LPS Rc P. typhimurium
SL684 Sigma +++++
+++++
+++++
++++

LPS Rc P. aeruginosa
PAC605 Univ. Edinburgh
- - - -

LPS RcP.sup.--
S. minnesota
R5 List ++++++
+++++
+++++
+++

LPS Rd2 E. coli
F583 Sigma +++ ++ - -

LPS Rd1P.sup.--
S. minnesota
R7 List - - - -

LPS Rd2 S. minnesota
R4 Institut Borstel
- - - -

LPS Re E. coli
K12 (D31m4) List - - - -

LPS Re E. coli

F515 Institut Borstel
- - - -
LPS Re S. minnesota
R595 List - - - -
LPS Re S. typhimurium
SL1102 Univ. Edinburgh
- - - -
LPS Re S. typhimurium
SL1181 Sigma - - - -
Lipid A E. coli
K12 (ex-D31m4)
List - - - -
Lipid A S. minnesota
R595 List + ++ - -
BSA - - - -

Purified native ***LPS*** (2 .mu.g/ml) were used to coat the plates
Values are reported as O.D., one + equals 0.5 O.D. (405 nm).

. . .

DETD TABLE IID

SZ 27 19.16.7

CHEMOTYPE	STRAIN	SUPPLIER	1 .mu.g/ml	100 ng/ml	10 ng/ml	1 ng/ml
LPS Smooth E. coli	02	Univ. Edinburgh	++	+	-	-
LPS Smooth E. coli	06	Univ. Edinburgh	-	-	-	-
LPS Smooth E. coli	012	Univ. Edinburgh	+++++	++++++	++++ +	
LPS Smooth E. coli	015	Univ. Edinburgh	+	+++	++	-
LPS Smooth E. coli	016	Univ. Edinburgh	-	-	-	-
LPS Smooth E. coli	018K-	Univ. Edinburgh	+	+++	-	-

LPS Smooth
E. coli
018K+ Univ. Edinburgh
++++ ++++ ++ -
LPS Smooth
E. coli
026B6 Difco +++++
+++++
+++ -
LPS Smooth
E. coli
055B5 Difco - - - -
LPS Smooth
E. coli
075 Univ. Edinburgh
+ + - -
LPS Smooth
E. coli
086 Univ. Edinburgh
++ ++++ +++ -
LPS Smooth
E. coli
0111B4 Difco +++++
+++++
+++++
+
LPS Smooth
E. coli
0127B8 Difco ++++++
+++++
+++++
+
LPS Smooth
E. coli
0128B12 Difco - - - -
LPS Smooth
E. coli
K235 List +++ ++ ++ -
LPS Smooth
S. minnesota
wt List ++ - - -
LPS Smooth
S. typhimurium
wt Difco +++++
+++++
+++ -
LPS cCore
E. coli
K12 Univ. Edinburgh
+++++
+++++
+++++
+
LPS cCore

E. coli
C62 Univ. Edinburgh
+++++
+++++
+++++
+

LPS cCore
E. coli
R1 Institut Borstel
+++++
+++++
+++++
+

LPS cCore
E. coli
R2 Institut Borstel
++++++
+++++
+++++
+

LPS cCore
E. coli
R3 Institut Borstel
+++++
+++++
+++++
+

LPS cCore
E. coli
R4 Institut Borstel
+++++
+++++
+++++
+

LPS cCore
S. minnesota
Ra R60 List +++++
+++++
+++++
+

LPS cCore
S. typhimurium
TV119 Sigma +++++
+++++
++ -

LPS cCore
S. typhimurium
1542 Univ. Edinburgh
+++++
+++++
++++ +

LPS cCore
K. aerogenes
M10B Univ. Edinburgh

- - - -

LPS Rb2 S. minnesota
R345 List +++++
++++ ++ -

LPS Rc E. coli
J5 List +++++
+++++
+++++
+

LPS Rc S. typhimurium
878 Univ. Edinburgh
+++++
+++++
+++++
+

LPS Rc P. typhimurium
SL684 Sigma ++++++
+++++
+++++
+

LPS Rc P. aeruginosa
PAC605 Univ. Edinburgh
+ - - -

LPS RcP.sup.-
S. minnesota
R5 List +++++
+++++
++++ +

LPS Rd2 E. coli
F583 Sigma - - - -

LPS Rd1P.sup.-
S. minnesota
R7 List - - - -

LPS Rd2 S. minnesota
R4 Institut Borstel
- - + +

LPS Re E. coli
K12 (D31m4) List - - - -

LPS Re E. coli
F515 Institut Borstel
- - - -

LPS Re S. minnesota
R595 List - - - -

LPS Re S. typhimurium
SL1102 Univ. Edinburgh
- - - -

LPS Re S. typhimurium
SL1181 Sigma - - - -

Lipid A E. coli
K12 (ex-D31m4)
List - - - -

Lipid A S. minnesota
R595 List - - - -

BSA - - - -

Purified native ***LPS*** (2 .mu.g/ml) were used to coat the plates
Values are reported as O.D., one + equals 0.5 O.D. (405 nm).

. . .

CLM What is claimed is:

1. A monoclonal antibody which binds an epitope in the core region of the ***LPS*** molecule and which is cross-reactive to, and cross-protective against endotoxemia caused by, at least two different Gram-negative bacterial strains having different core structures, said bacterial strains selected from the group consisting of: (a) smooth E. coli, (b) ***rough*** mutant E. coli of core types R1, R2, R3, R4 and K12; and (c) Salmonella; said monoclonal antibody having a. . .

. . . an epitope which is completely present in the Rc core structure of E. coli and is also present in the ***complete*** ***core*** .

. . . antibody according to claim 1 characterized by the steps of a) Immunizing an animal with a plurality of types of ***LPS*** molecule b) Fusing spleen cells from the animal with an immortalizing cell line to produce hybridomas c) Screening the hybridomas. . .

7. A method according to claim 6 in which the animal is immunized with a cocktail of different ***rough*** strains of heat-killed Gram-negative bacteria.

8. A method according to claim 6 in which the animal is immunized sequentially with a number of different ***rough*** strains of heat-killed Gram- negative bacteria, only one strain being administered at any one time.

. . . the screening step c) is carried out in an ELISA assay using a series of mixtures of different smooth and ***rough*** ***LPS*** types.

11. An ***LPS*** binding molecule which comprises at least one antigen binding site comprising at least one domain which comprises in sequence framework. . . Asp Tyr which are amino acids 101-109 of SEQ ID NO:2 or SEO ID NO:4; and direct equivalents thereof, said ***LPS*** binding molecule which binds an epitope in the core region of the ***LPS*** molecule of gram negative bacterial strains having different core structures and selected from the group consisting of smooth E. coli; ***rough*** E. coli of core types R1, R2, R3, R4 and K12; and Salmonella.

13. An ***LPS*** binding molecule according to claim 11 comprising at least one antigen binding site comprising: a) a first domain comprising the. . .

14. An ***LPS*** binding molecule according to claim 13 in which the hypervariable regions are associated with murine or human framework regions.

15. An ***LPS*** binding molecule according to claim 13 in which the first and the second domains are part of a single common. . .

16. An ***LPS*** binding molecule according to claim 15 in which the first and the second domains are respectively an Ig heavy chain. . .

17. An ***LPS*** binding molecule according to claim 13 in which the first domain is part of a heavy chain of at least. . .

18. An ***LPS*** binding molecule according to claim 17 which is a complete Ig molecule.

25. An ***LPS*** binding molecule according to any one of claims 11-24 for use as a pharmaceutical agent.

26. A pharmaceutical composition comprising an ***LPS*** binding molecule according to any one of claims 11-24 in association with a pharmaceutically acceptable diluent or carrier.

=> dup rem l13
PROCESSING COMPLETED FOR L13
L15 38 DUP REM L13 (87 DUPLICATES REMOVED)

=> d bib ab kwic 1-
YOU HAVE REQUESTED DATA FROM 38 ANSWERS - CONTINUE? Y/(N):y

L15 ANSWER 1 OF 38 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 1
AN 2000:534435 BIOSIS
DN PREV200000534435
TI Preparation and preclinical evaluation of a novel liposomal ***complete*** - ***core*** ***lipopolysaccharide*** vaccine.
AU Bennett-Guerrero, Elliott (1); McIntosh, Thomas J.; Barclay, G. Robin; Snyder, D. Scott; Gibbs, Richard J.; Mythen, Michael G.; Poxton, Ian R.
CS (1) Department of Anesthesiology, Columbia University College of Physicians and Surgeons, 630 W. 168th St., New York, NY, 10032-3784 USA
SO Infection and Immunity, (November, 2000) Vol. 68, No. 11, pp. 6202-6208. print.
ISSN: 0019-9567.
DT Article
LA English
SL English
AB Our objective is to develop a prophylactic vaccine strategy that can be evaluated for surgical and other high-risk hospitalized patients. In this paper, we describe the preparation and preclinical evaluation of a liposomal ***complete*** - ***core*** ***lipopolysaccharide*** (***LPS***) vaccine that is nontoxic and broadly antigenic. ***Complete*** - ***core*** (Ra-chemotype) LPSs were isolated from four gram-negative bacterial strains (Escherichia coli K-12, E. coli R1, Pseudomonas aeruginosa PAC608, and Bacteroides fragilis), mixed together to form a cocktail of ***complete*** - ***core*** LPSs, and then incorporated into multilamellar liposomes consisting of dimyristoyl phosphatidyl choline, dimyristoyl phosphatidylglycerol, and cholesterol in a 4:1:4 molar ratio. The endotoxic activities of these ***LPS*** -containing liposomes were less than 0.1% of the endotoxicities of the original free LPSs as measured by the Limulus amoebocyte lysate assay. In vivo administration of liposomal ***complete*** - ***core*** ***LPS*** mixed with Al(OH)3 to rabbits resulted in no pyrogenicity or overt toxicity over a 7-day period. In immunoblots, sera from rabbits following active immunization elicited cross-reactive antibodies to a large panel of ***rough*** and smooth LPSs from numerous clinically

relevant gram-negative bacteria, including E. coli (serotypes O1, O4, O6, O8, O12, O15, O18, O75, O86, O157, and O111), P. aeruginosa (Fisher-Devlin serotypes 1, 2, and 3, which correspond to International Antigenic Typing Scheme types 6, 11, and 2, respectively), Klebsiella pneumoniae (serotypes O1, O2ab, and O3), B. fragilis, and Bacteroides vulgatus. Active immunization of mice with liposomal ***complete*** - ***core*** ***LPS*** provided protection against a lethal challenge with E. coli O18 ***LPS*** . The vaccine tested was nontoxic, nonpyrogenic, and immunogenic against a wide variety of pathogens found in clinical settings.

TI Preparation and preclinical evaluation of a novel liposomal ***complete*** - ***core*** ***lipopolysaccharide*** vaccine.

AB. . . for surgical and other high-risk hospitalized patients. In this paper, we describe the preparation and preclinical evaluation of a liposomal ***complete*** - ***core*** ***lipopolysaccharide*** (***LPS***) vaccine that is nontoxic and broadly antigenic. ***Complete*** - ***core*** (Ra-chemotype) LPSs were isolated from four gram-negative bacterial strains (Escherichia coli K-12, E. coli R1, Pseudomonas aeruginosa PAC608, and Bacteroides fragilis), mixed together to form a cocktail of ***complete*** - ***core*** LPSs, and then incorporated into multilamellar liposomes consisting of dimyristoyl phosphatidyl choline, dimyristoyl phosphatidylglycerol, and cholesterol in a 4:1:4 molar ratio. The endotoxic activities of these ***LPS*** -containing liposomes were less than 0.1% of the endotoxicities of the original free LPSs as measured by the Limulus amoebocyte lysate assay. In vivo administration of liposomal ***complete*** - ***core*** ***LPS*** mixed with Al(OH)3 to rabbits resulted in no pyrogenicity or overt toxicity over a 7-day period. In immunoblots, sera from rabbits following active immunization elicited cross-reactive antibodies to a large panel of ***rough*** and smooth LPSs from numerous clinically relevant gram-negative bacteria, including E. coli (serotypes O1, O4, O6, O8, O12, O15, O18,. . . 2, respectively), Klebsiella pneumoniae (serotypes O1, O2ab, and O3), B. fragilis, and Bacteroides vulgatus. Active immunization of mice with liposomal ***complete*** - ***core*** ***LPS*** provided protection against a lethal challenge with E. coli O18 ***LPS*** . The vaccine tested was nontoxic, nonpyrogenic, and immunogenic against a wide variety of pathogens found in clinical settings.

IT Major Concepts
Immune System (Chemical Coordination and Homeostasis); Infection; Pharmacology

IT Chemicals & Biochemicals
cholesterol; dimyristoyl phosphatidyl choline; dimyristoyl phosphatidylglycerol; ***lipopolysaccharide*** vaccine: liposomal ***complete*** - ***core*** , preclinical evaluation, preparation, vaccine

L15 ANSWER 2 OF 38 BIOSIS COPYRIGHT 2001 BIOSIS DUPLICATE 2

AN 2000:226563 BIOSIS

DN PREV200000226563

TI ***Rough*** and smooth forms of fluorescein-labelled bacterial endotoxin exhibit CD14/LBP dependent and independent binding that is influenced by endotoxin concentration.

AU Triantafilou, Martha; Triantafilou, Kathy (1); Fernandez, Nelson

CS (1) Department of Biological Sciences, University of Essex, Wivenhoe Park, Central Campus, Colchester, Essex, CO4 3SQ UK
SO European Journal of Biochemistry, (April, 2000) Vol. 267, No. 8, pp. 2218-2226.
ISSN: 0014-2956.
DT Article
LA English
SL English
AB ***Lipopolysaccharide*** (***LPS*** , or endotoxin), is a major constituent of the outer membrane of Gram-negative bacteria. Bacteria express either smooth ***LPS*** , which is composed of O-antigen (O-Ag), ***complete*** ***core*** oligosaccharides, and the lipid A, or ***rough*** ***LPS*** which lack O-Ag but possess lipid A and progressively shorter core oligosaccharides. CD14 has been described as the receptor for complexes of ***LPS*** with ***LPS*** -binding protein (LBP). Using flow cytometry we have compared the binding of Salmonella minnesota ***rough*** ***LPS*** (ReLPS) and Escherichia coli smooth ***LPS*** labelled with fluorescein isothiocyanate (FITC- ***LPS***) to Chinese hamster ovary (CHO) cells transfected with human CD14 gene (hCD14-CHO), to MonoMac 6 cells and to endothelial cells. Our results showed that both forms of ***LPS*** display the same binding characteristics, and that the binding of FITC- ***LPS*** to cells was both CD14- and LBP-dependent for ***LPS*** concentrations up to 100 ngcntdotmL-1. At ***LPS*** concentrations higher than 100 ngcntdotmL-1 we observed CD14/LBP-independent binding. CD14/LBP-dependent binding was dose dependent, saturable, and enhanced in the presence of human pooled serum (HPS), and the monoclonal anti-CD14 antibody (MY4) or unlabelled ***LPS*** could outcompete it.
TI ***Rough*** and smooth forms of fluorescein-labelled bacterial endotoxin exhibit CD14/LBP dependent and independent binding that is influenced by endotoxin concentration.
AB ***Lipopolysaccharide*** (***LPS*** , or endotoxin), is a major constituent of the outer membrane of Gram-negative bacteria. Bacteria express either smooth ***LPS*** , which is composed of O-antigen (O-Ag), ***complete*** ***core*** oligosaccharides, and the lipid A, or ***rough*** ***LPS*** which lack O-Ag but possess lipid A and progressively shorter core oligosaccharides. CD14 has been described as the receptor for complexes of ***LPS*** with ***LPS*** -binding protein (LBP). Using flow cytometry we have compared the binding of Salmonella minnesota ***rough*** ***LPS*** (ReLPS) and Escherichia coli smooth ***LPS*** labelled with fluorescein isothiocyanate (FITC- ***LPS***) to Chinese hamster ovary (CHO) cells transfected with human CD14 gene (hCD14-CHO), to MonoMac 6 cells and to endothelial cells. Our results showed that both forms of ***LPS*** display the same binding characteristics, and that the binding of FITC- ***LPS*** to cells was both CD14- and LBP-dependent for ***LPS*** concentrations up to 100 ngcntdotmL-1. At ***LPS*** concentrations higher than 100 ngcntdotmL-1 we observed CD14/LBP-independent binding. CD14/LBP-dependent binding was dose dependent, saturable, and enhanced in the presence of human pooled serum (HPS), and the monoclonal anti-CD14 antibody (MY4) or unlabelled ***LPS*** could outcompete it.
IT . . .
Biology; Toxicology
IT Parts, Structures, & Systems of Organisms

endothelial cell; serum: blood and lymphatics
IT Chemicals & Biochemicals
CD14; ***lipopolysaccharide*** -binding protein; ***rough*** ***lipopolysaccharide*** ; smooth ***lipopolysaccharide***

L15 ANSWER 3 OF 38 USPATFULL
AN 1999:155456 USPATFULL
TI Proteins involved in the synthesis and assembly of O-antigen in Pseudomonas aeruginosa
IN Lam, Joseph S., Guelph, Canada
Burrows, Lori, Guelph, Canada
Charter, Deborah, Guelph, Canada
de Kievit, Teresa, Guelph, Canada
PA University of Guelph, Guelph, Canada (non-U.S. corporation)
PI US 5994072 19991130
AI US 1997-846762 19970430 (8)
PRAI US 1996-16510 19960430 (60)
US 1997-39473 19970227 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Degen, Nancy; Assistant Examiner: Schwartzman, Robert
LREP Merchant & Gould P.C.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 66 Drawing Figure(s); 63 Drawing Page(s)
LN.CNT 7459
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Novel nucleic acid molecules encoding proteins involved in the synthesis and assembly of O-antigen in P. aeruginosa; and novel proteins encoded by the nucleic acid molecules are described. Methods are disclosed for detecting P. aeruginosa in a sample by determining the presence of the proteins or a nucleic acid molecule encoding the proteins in the sample.
SUMM . . . identified in the pathogenesis of P. aeruginosa infections, including proteins such as exotoxin A, proteases, and exopolysaccharides including alginate and ***lipopolysaccharide*** (***LPS***). The ***LPS*** of P. aeruginosa is typical of Gram-negative bacteria, composed of lipid A-core oligosaccharide-O antigen repeating units.
SUMM P. aeruginosa is capable of coexpressing two distinct forms of ***LPS*** , designated A-band and B-band ***LPS*** , respectively. A-band ***LPS*** is a shorter, common form expressed by the majority of P. aeruginosa serotypes, and has a trisaccharide repeating unit of .alpha.-D-rhamnose linked 1.fwdarw.3, 1.fwdarw.3, 1.fwdarw.2. B-band ***LPS*** is the serotype-specific, O-antigen-containing form, and is a heteropolymer composed of di- to pentasaccharide repeats containing a wide variety of. . .
SUMM . . . the cloning of genes involved in the expression of A-band (Lightfoot and Lam, 1991) and B-band (Lightfoot and Lam, 1993) ***LPS*** of P. aeruginosa. A recombinant cosmid clone pFV3 complemented A-band ***LPS*** synthesis in an A-band-deficient mutant, rd7513. pFV3 also mediated A-band ***LPS*** synthesis in five of the six P. aeruginosa O serotypes which lack A-band ***LPS*** . Another cosmid clone, pFV100, complemented B-band ***LPS*** synthesis in mutant ge6, which lacks B-band ***LPS*** . Physical mapping of the genes involved in A-band and B-band ***LPS***

synthesis indicated that the two gene clusters are physically distinct and are separated by more than 1.9 Mbp on the P. aeruginosa PAO1 genome. A-band ***LPS*** genes mapped between 5.75 and 5.89 Mbp (10.5 to 13.3 min), and B-band ***LPS*** genes mapped at 1.9 Mbp (near 37 min) on the 5.9-Mbp chromosome.

SUMM . . . linkage or one epimer from O5 (Knirel et al., 1988) (FIG. 30). Immunochemical cross reactions have also been demonstrated among ***LPS*** of serotypes O2, O5 and O16 by the use of monoclonal antibodies (Lam et al., 1992). The rfbA (herein also. . .

SUMM There are currently three pathways proposed for biosynthesis and assembly of ***LPS*** , the Rfc-dependent and Rfcindependent pathways. Rfc is the O-antigen polymerase, and appears to be required for assembly of heteropolymeric O-antigens. . . and Stocker, 1984). In contrast, homopolymeric O-antigens appear to be assembled without an O-antigen polymerase (Whitfield, 1995). Rfc-dependent (or Wzy) ***LPS*** synthesis has been shown to involve at least two other gene products which act in concert with Rfc; RfbX (or. . .

SUMM The present inventors have characterized a P. aeruginosa B-band (psb) gene cluster involved in the synthesis and assembly of B-band ***lipopolysaccharide*** i.e. O-antigen. The gene cluster is also known as and referred to herein as the wbp gene cluster.

SUMM . . . as wbpM and wbpN respectively ("Group II genes"). The psb gene cluster also contains genes which are not involved in ***LPS*** synthesis including the genes rpsA and himD and the novel genes designated uvrB, insertion element IS407, hisH and hisF. The. . .

SUMM . . . psbI (wbpI), psbJ (wbpJ), psbK (wbpK), psbL (wbpL), psbM (wbpM), and psbN (wbpN) involved in the synthesis, and assembly of ***lipopolysaccharide*** in P. aeruginosa. The terms in parenthesis correspond to other designations that have been given to these genes. The gene cluster may also contain the non- ***LPS*** gene uvrB, the insertion element IS407 (IS1209), the genes hisH and hisF involved in histidine synthesis, the gene rpsA which. . .

DRWD FIG. 22A shows a silver-stained SDS-PAGE gel of ***LPS*** from PAO1, AK14O1, AK14O1(pFV100), and AK14O1(pFV.TK8) [(Panel A) and Western immunoblots of this ***LPS*** reacted with O5-specific MAb MF15-4 (Panel B)];

DRWD FIG. 22B shows a Western immunoblots of this ***LPS*** reacted with O5-specific MAb MF15-4;

DRWD FIG. 25A shows a silver-strained SDS-PAGE gel ***LPS*** from PAO1, AK14O1 and the three rfc (wzy) chromosomal mutants, PO5.2, OP5.3, and OP5.5;

DRWD FIG. 25B shows a Western blot of ***LPS*** from PAO1, AK14O1 and the three rfc (wzy) chromosomal mutants PO5.2, OP5.3, and 0P5.5;

DRWD FIG. 28A shows a Western immunoblot[s] which illustrates a characterization of ***LPS*** from PAO1 and PAO1 rol (wzz) chromosomal mutant where the blot is silver-stained SDS-PAGE gel;

DRWD FIG. 28B shows a Western immunoblot which illustrates a characterization of ***LPS*** from PAO1 and PAO1 rol (wzz) chromosomal mutant where the immunoblot was reacted with an O5 (B-band)-specific mAb MF15-4;

DRWD FIG. 46A shows an SDS-PAGE gel of ***LPS*** from Wzz knockout mutants;

DETD . . . psbI (wbpI), psbJ (wbpJ), psbK (wbpK), psbL (wbpL), psbM (wbpM), and psbN (wbpN) involved in the synthesis, and assembly of ***lipopolysaccharide*** in P. aeruginosa. The gene cluster may also

contain the non- ***LPS*** genes hisH, hisF, himD, rspa, uvrB, and the insertion element IS407 (IS1209).

DETD . . . Using a novel gene-replacement vector, the present inventors were able to generate PAO1 chromosomal rfc mutants. These knockout mutants express ***LPS*** containing ***complete*** ***core*** plus one O-repeat unit, indicating that they are no longer producing a functional O-polymerase enzyme.

DETD . . . most preferably comprises nucleotides 19678-21675 as shown in FIG. 2 or SEQ.ID. No.: 1. PsbM knockout mutants do not produce ***LPS*** .

DETD . . . A and B synthesis are knocked out indicating that its gene product is required for expresser of A and B-band ***LPS*** onto the core oligosaccharide. Accordingly, the invention provides a nucleic acid molecule encoding a PsbF (WpbF) protein and an Rfc. . .

DETD . . . more detail below. The primers may be used to amplify the genomic DNA of other bacterial species known to have ***LPS*** . The PCR amplified sequences can be examined to determine the relationship between the various ***LPS*** genes.

DETD . . . O-antigen is a virulence factor of P. aeruginosa and it is responsible for serum resistance. Therefore, substances which can target ***LPS*** biosynthesis in P. aeruginosa to change the organism into making " ***rough*** " ***LPS*** devoid of the long chain O-antigen (B-band) polymers will be useful in rendering the bacterium susceptible to attack by host. . .

DETD Preparation of ***LPS***

DETD ***LPS*** used in sodium dodecyl sulfate-polyacrylamide gel electrophoresis (SDS-PAGE) and Western immunoblotting experiments was prepared according to the proteinase K digest. . .

DETD The discontinuous SDS-PAGE procedure of Hancock and Carey (1979) utilizing 15% running gels was used. ***LPS*** separated by SDS-PAGE was visualized by silver-staining according to the method of Dubray and Bezard (1982).

DETD . . . blocked with 3% (w/v) skim milk followed by incubation with hybridoma culture supernatant containing either MAb MF15-4, specific for O5 ***LPS*** , or MAb N1F10, specific for A-band ***LPS*** . The blots were developed at room temperature, using goat anti-mouse F(ab').sub.2 fragment conjugated antibody (Jackson Immunoresearch Laboratories, West Grove, Pa.). . .

DETD Analysis of the ***LPS*** from mutants AK14O1 and rd7513. Strain AK14O1 has been previously shown to contain A-band ***LPS*** ; its B-band ***LPS*** consists of ***complete*** ***core*** plus one O-repeat unit (SR phenotype) (Berry and Kropinski, 1986; Lam et al., 1992). Strain rd7513 is a mutant of AK14O1 that has the SR phenotype but is no longer producing A-band ***LPS*** , due to a mutation in an A-band biosynthetic gene (Lightfoot and Lam, 1991). Strain rd7513 was used in this study. . .

DETD . . . Mobilization of pFV100, which contains the O5 rfb gene cluster, into SR mutant AK14O1 resulted in production of O5 B-band ***LPS*** . These results suggest that an O-polymerase gene might be localized on the cloned DNA. Analysis of ***LPS*** isolated from PAO1 and AK14O1(pFV100) in both silver-stained SDS-PAGE gels and Western immunoblots, reacted with O5-specific MAb MF15-4, revealed that the two strains expressed similar high molecular weight ***LPS*** profiles (FIG. 22 a, b). In order to localize the putative rfc gene on the 26 kb

insert of pFV100,. . .

DETD . . . 23). This 1.5 kb XhoI fragment was cloned into vector pUCP26 (pFV.TK7) and mobilized into AK14O1. In Western immunoblots of ***LPS*** from AK14O1(pFV.TK7) with MAb MF15-4 no reaction of this antibody with high molecular weight B-band ***LPS*** could be detected (data not shown). Therefore, the 1.5 kb XhoI insert in pFV.TK7 was unable to restore the O-polymerase. . . Silver-stained SDS-PAGE gels and Western blots reacted with MAb MF15-4, showed that the AK14O1(pFV.TK8) transconjugants expressed levels of O5 B-band ***LPS*** comparable to that produced by the wild-type PAO1 (FIG. 22).

DETD . . . PAO1 control DNA (FIG. 24c, lane 1), demonstrating that gene replacement had occurred in OP5.2, OP5.3, and OP5.5. Analysis of ***LPS*** from these three strains in silver-stained gels and Western immunoblots with O5-specific MAb MF15-4 demonstrated that they were not capable. . . reacted with A-band specific MAb N1F10 revealed that, like the SR mutant AK14O1, these three mutants were still producing A-band ***LPS*** (FIG. 25c). Biosynthesis of A-band ***LPS*** therefore, appears to be unaffected by this chromosomal mutation. The relative mobility of the core-lipid A bands was also similar to that of the SR mutant AK14O1 (FIG. 25a); therefore the ***LPS*** phenotype of the three rfc knockout mutants was identical to that of AK14O1. Mobilization of pFV.TK8 into OP5.2, OP5.3 and. . .

DETD . . . O5 encoding an O-polymerase enzyme. Using a gene-replacement system, P. aeruginosa rfc-chromosomal mutants were generated which expressed the typical sr ***lps*** phenotype. The P. aeruginosa Rfc is similar to other reported Rfc proteins in that it is very hydrophobic, containing 11. . .

DETD The ***LPS*** of the mutants was prepared according to the proteinase K digest method of Hitchcock and Brown (1983). The ***LPS*** was analyzed using sodium dodecyl sulfate polyacrylamide gel electrophoresis (SDS-PAGE) and Western immunoblots according to the methods described previously (de Kievit et al., 1995). When compared with the wild-type strain, the mutant ***LPS*** showed a marked alteration in the O-antigen ladder-like banding pattern, in which there was a decrease in high molecular weight. . .

DETD . . . a protein which regulates O-antigen chain length. Using a gene-replacement system, P. aeruginosa rol::Gm.sup.R knockout mutants were generated which express ***LPS*** with unregulated O-antigen chain length. Thus, the P. aeruginosa O5 (PAO1) Rol protein has both sequence and functional homology to other reported Rol proteins. This also confirms that the pathway for P. aeruginosa B-band ***LPS*** biosynthesis is Rfc-dependent. The function of Rol is often associated with the Rfc protein, an O-polymerase (Whitfield, 1995, Kievit et. . .

DETD . . . ORFs with high homology to other bacterial genes or insertion sequences but which are not thought to be involved with ***LPS*** synthesis were identified (hisH, hisF, uvrB, IS407; Table 1).

DETD . . . two ORFs (psbM and psbN or sometimes referred to as the Group II genes) which may be involved in O5 ***LPS*** biosynthesis (see below).

DETD . . . 5' end of pFV100. Preliminary sequence analysis of this upstream region revealed no additional ORFs thought to be involved with ***LPS*** synthesis. Also, no insertion sequences could be found in this region of DNA. Localization of the 5' end of the. . .

DETD Sequence analysis of pFV100/pFV400 revealed no homology to gnd (encoding

6-phosphogluconate dehydrogenase) in the regions flanking the ***LPS*** genes. However, P. aeruginosa has been shown to convert glucose-6-phosphate to 6-phosphogluconate as part of the Entner-Douderoff pathway, suggesting a. . .

DETD . . . has been cloned from an overlapping cosmid, pFV400, and its function confirmed by mutational analysis (Example 2). In other Rfc-dependent ***LPS*** gene clusters, the rol gene is positioned near or at the end of the cluster. These results, along with the. . .

DETD . . . (Meier-Dieter et al., 1992). ECA is an exopolysaccharide common to most enterics that can be linked to lipid A-core in ***rough*** strains. It is composed of N-acetyl-D-glucosamine (GlcNAc), N-acetyl-D-mannosaminuronic acid (ManNAcA), and 4-acetamido-4,6-dideoxy-D-galactose (Fuc4NAc).

DETD . . . for puromycin production (Tercero et al., 1996). PsbB has 17% homology to the BplA protein from B. perttussis required for ***LPS*** production (Allen and Maskell, 1996) and even weaker homology to ORF334 and MocA from Rhizobium meliloti found in the operon. . .

DETD . . . of the psb genes were found to have high homology with bpl genes, suggesting a common ancestry. B. pertussis has semi- ***rough*** ***LPS*** , with only one O-antigen unit attached to the core oligosaccharide. The composition of the B. pertussis O-antigen unit is N-acetylglucosamine. . .

DETD . . . The product of the psbD gene is most homologous with the product of the bplB gene in the B. pertussis ***LPS*** biosynthetic cluster (Allen and Maskell, 1996). PsbD and BplB appear to be O-acetyl transferases, and have some homology to serine. . .

DETD psbE has high homology with a B. pertussis ***LPS*** biosynthetic gene, bplC. psbD and psbE are adjacent to one another in the psb cluster, as are bplB and bplC. . .

DETD . . . cassette into rfc were used to confirm this gene encoded the O-antigen polymerase. Gentamicin-resistant mutants were shown to have the semi- ***rough*** phenotype (See Example 1) characteristic of an rfc mutant (Makela and Stocker, 1984).

DETD . . . (reviewed in Schnaitman and Klena, 1993). Comparison of the chromosomal map locations of the P. aeruginosa O5 A- and B-band ***LPS*** clusters with those of known PAO1 his mutations showed there were no his genes located adjacent to either the psa. . .

DETD . . . (Table 1). PsbM mutants, generated by insertion of a gentamicin cassette into a unique NruI site within psbM, exhibit B-band ***LPS*** -minus phenotype. This confirms the involvement of the psbM product in ***LPS*** biosynthesis, despite the fact it lies outside of the O5-specific region (FIG. 41). PsbM has homology to a range of proteins involved in exopolysaccharide synthesis, including BpIL from the B. pertussis ***LPS*** cluster (Allen and Maskell, 1996), TrsG from the core biosynthetic cluster of Y. enferocolitica O3 (Skurnik et al., 1995), and. . .

DETD . . . fusion protein. In support of this hypothesis, PsbM also has homology to two adjacent ORFs (ORF10 and ORF11) in the ***LPS*** cluster of V. cholerae O139 (Comstock et al., 1996). The homology to ORF10 and ORF11 lies in the amino-terminal and. . .

DETD Preparation and Visualization of ***LPS*** .

DETD ***LPS*** from P. aeruginosa was prepared by the method of Hitchcock and Brown, 1983. The ***LPS*** preparations were separated on standard discontinuous 12.5% SDS-PAGE gels and visualized by silver

* * * * * * * * * * * * * STN Columbus * * * * * * * * * * * * * *
FILE 'HOME' ENTERED AT 06:53:38 ON 27 SEP 2001
=> file biosis, caba, caplus, embase, japio, lifesci, medline, scisearch, uspatfull
=> s l1 and (Ra or Rb or Rc or Rd or Re)
L2 60 L1 AND (RA OR RB OR RC OR RD OR RE)
=> d 60 bib ab kwic

L2 ANSWER 60 OF 60 USPATFULL
AN 90:42500 USPATFULL
TI Lipopolysaccharides of reduced toxicity and the production thereof
IN Munford, Robert S., Dallas, TX, United States
Hall, Catherine L., Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 4929604 19900529
AI US 1986-868428 19860528 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Wiseman, Thomas G.; Assistant Examiner: Patterson, Jr., Charles L.
LREP Arnold, White & Durkee
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 709
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An acyloxyacyl hydrolase from the human promyelocyte cell line HL-60 has been found to specifically hydrolyze fatty acids form their ester linkages to hydroxy groups of 3-hydroxyfatty acids, the latter being bound in turn to LPS glycosaminyl residues. The hydrolyzed fatty acids may include dodecanoic acid, tetradecanoic acid and hexadecanoic acid. This enzyme showed a molecular weight between about 50,000 daltons and about 70,000 daltons.

Altered bacterial LPS substantially without fatty acids bound in ester linkage to hydroxy groups of 3-hydroxyfatty acids covalently linked to a glucosaminyl moiety of LPS lipid A are produced. Since the structure of the lipid A moiety is highly conserved, acyloxyacyl hydrolase may act on LPS of many different pathogenic bacteria (for example Salmonella, Escherichia, Hemophilus, and Neisseria).

Such altered bacterial LPS, having toxicity reduced more than immunostimulatory activity, may be therapeutically useful: (1) as ***vaccines*** to prevent Gram-negative bacterial diseases by inducing antibodies to LPS 0-polysaccharide or R-core antigens, (2) as antidotes to treat or prevent gram-negative bacterial sepsis ("septic shock"), or (3) as adjuvants to enhance formation of antibodies to other antigens. The acyloxyacyl hydrolase itself may be therapeutically useful to detoxify endogenous LPS in patients with gram-negative bacterial diseases or to remove toxic LPS from therapeutic injectants.
AB Such altered bacterial LPS, having toxicity reduced more than immunostimulatory activity, may be therapeutically useful: (1) as ***vaccines*** to prevent Gram-negative bacterial diseases by inducing antibodies to LPS 0-polysaccharide or R-core antigens, (2) as antidotes

to treat or. . .

SUMM . . . reduced more than immunostimulatory activity, may be therapeutically useful. Such therapeutic usefulness comprises use of the altered LPS (1) as ***vaccines*** to prevent gramnegative bacterial diseases by inducing antibodies to O-polysaccharide or R-core antigens, (2) as antidotes to treat or prevent. . .

DRWD . . . smooth LPS (i.e., containing O-antigen). R-LPS refers to rough LPS. The R-core is further subdivided, according to its length, from ***Ra*** (complete core) to ***Re*** (only 2-keto-3-deoxy-octulosonic acid (KDO)). The term "deep-rough" LPS refers to ***Re*** LPS. SR-LPS have one O-antigen repeat unit attached to the R-core.

DRWD . . . SR-LPS (0.6% deacylated); lane 4, SR-LPS (15%); lane 5, SR-LPS (28%); lane 6, SR-LPS (65% deacylated with NaOH); lane 7, ***Rc*** -LPS (1%); lane 8, ***Rc*** -LPS (20%); lane 9, ***Rc*** -LPS (32%); lane 10, ***Rc*** -LPS (65% deacylated with NaOH); and lane 11, S-LPS (1%). The LPS in lanes 6 and 10 were deacylated by treatment. . .

DRWD . . . substrate. Nonradioactive LPS from S. minnesota were added (adjusted to 0.27 umoles) to reaction mixtures that contained 0.27 umoles radiolabeled ***Rc*** -LPS. After incubation at 37.degree. C. for 9 hours, the amount of released .sup.3 H-fatty acid was determined by extracting the fatty acids into chloroform and counting. The nonradioactive LPS had approximately 6 (***Rc***), 9 (***Rb***), 10 (***Ra***), and 14-50 (smooth) saccharides attached to lipid A.

DETD . . . not altered by acyloxyacyl hydrolysis. Enzymatic detoxification of lipid A without destruction of immunostimulatory activity may thus produce non-toxic LPS ***vaccines*** ; the adjuvanticity of the detoxified lipid A would help promote the formation of antibodies to the polysaccharide antigen(s). As noted. . .

DETD . . . In addition, a lipid A analog that structually resembles the product of acyloxyacyl hydrolysis has been shown capable of reversing ***endotoxic*** ***shock*** in mice and sheep (Clin. Res., V 34, p 518A, 1986). Detoxified LPS may be superior to lipid A analogs. . .

DETD . . . supernatants were counted and the percentage of each radiolabel that appeared in the supernatant was calculated. .sup.32 P-labeled S. typhimurium ***Rc*** LPS, prepared by growing strain PRX20 in a low phosphate medium that contained .sup.32 PO.sub. 4 (orthophosphate, New England Nuclear,. . .

DETD . . . may artifactually influence this molecular weight estimate. The enzyme preparation did not contain phosphatases that acted on either S. typhimurium ***Rc*** -LPS or on a deep-rough E. coli LPS. Analysis of the enzyme hydrolysis product by thin-layer chromatography of the fatty acids. . .

DETD . . . experiments, when LPS with different polysaccharide chain lengths were radiolabeled and used as substrates for the enzyme, the shortest-chain LPS (***Re***) underwent significantly less hydrolysis than did the longer-chain LPS (Smooth, ***Rc***). Thus acyloxyacyl hydrolase was more active in vitro on LPS substrates with long polysaccharide chains.

DETD . . . were derived by applying the results of 10-fold dilutions of test samples to a standard curve that was constructed with ***Rc*** LPS, with normalization to a starting concentration of 10 ug/ml. Dilutions were performed in pyrogen-free water. Each value is the. . .

CLM What is claimed is:

7. A method of ***vaccinating*** an animal to prevent Gram-negative bacterial diseases or treating animals with Gram-negative bacterial diseases, the method consisting essentially of administering. . .

. . . 9. A method for prophylactically treating an animal to prevent a particular Gram-negative bacterial disease, the method consisting essentially of ***vaccinating*** said animal, in an amount sufficient to produce immunity, with a lipopolysaccharide obtained from the particular Gram-negative bacterium and modified. . .

. . . 10. A method for prophylactically treating an animal to prevent a given Gram-negative bacterial disease, the method consisting essentially of ***vaccinating*** said animal with an amount sufficient to produce immunity of a lipopolysaccharide obtained from a Gram-negative bacterium of a type. . .

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 59 DUP REM L2 (1 DUPLICATE REMOVED)

=> s l1 and (R1 or R2 or R3 or R4 or K12)
L4 26 L1 AND (R1 OR R2 OR R3 OR R4 OR K12)

=> d bib ab l3

L3 ANSWER 1 OF 59 USPATFULL
AN 2001:145278 USPATFULL
TI Modified vitamin K-dependent polypeptides
IN Nelsestuen, Gary L., St. Paul, MN, United States
PA Regents of the University of Minnesota, a Minnesota corporation (U.S. corporation)
PI US 2001018414 A1 20010830
AI US 2001-803810 A1 20010312 (9)
RLI Continuation of Ser. No. US 1999-302239, filed on 29 Apr 1999, PENDING Continuation-in-part of Ser. No. US 1997-955636, filed on 23 Oct 1997, GRANTED, Pat. No. US 6017882
DT Utility
FS APPLICATION
LREP MARK S. ELLINGER, PH.D., Fish & Richardson P.C., P.A., Suite 3300, 60 South Sixth Street, Minneapolis, MN, 55402
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 1784
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides vitamin k-dependent polypeptides with enhanced membrane binding affinity. These polypeptides can be used to modulate clot formation in mammals. Methods of modulating clot formation in mammals are also described.

=> d bib ab l3 1-
YOU HAVE REQUESTED DATA FROM 59 ANSWERS - CONTINUE? Y/(N):y

L3 ANSWER 1 OF 59 USPATFULL

AN 2001:145278 USPATFULL
TI Modified vitamin K-dependent polypeptides
IN Nelsestuen, Gary L., St. Paul, MN, United States
PA Regents of the University of Minnesota, a Minnesota corporation (U.S. corporation)
PI US 2001018414 A1 20010830
AI US 2001-803810 A1 20010312 (9)
RLI Continuation of Ser. No. US 1999-302239, filed on 29 Apr 1999, PENDING Continuation-in-part of Ser. No. US 1997-955636, filed on 23 Oct 1997, GRANTED, Pat. No. US 6017882
DT Utility
FS APPLICATION
LREP MARK S. ELLINGER, PH.D., Fish & Richardson P.C., P.A., Suite 3300, 60 South Sixth Street, Minneapolis, MN, 55402
CLMN Number of Claims: 22
ECL Exemplary Claim: 1
DRWN 15 Drawing Page(s)
LN.CNT 1784
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides vitamin k-dependent polypeptides with enhanced membrane binding affinity. These polypeptides can be used to modulate clot formation in mammals. Methods of modulating clot formation in mammals are also described.

L3 ANSWER 2 OF 59 USPATFULL
AN 2001:114616 USPATFULL
TI METHOD FOR THE AUGMENTATION OF GENE EXPRESSION
IN MOUNTZ, JOHN D., BIRMINGHAM, AL, United States
ZHANG, HUANG-GE, BIRMINGHAM, AL, United States
ZHOU, TONG, BIRMINGHAM, AL, United States
EDWARDS, CARL K., III, SUPERIOR, CO, United States
PI US 2001008881 A1 20010719
AI US 1998-187952 A1 19981106 (9)
PRAI US 1997-64694 19971107 (60)
DT Utility
FS APPLICATION
LREP BENJAMIN A. ADLER, 8011 CANDLE LANE, HOUSTON, TX, 77071
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 9 Drawing Page(s)
LN.CNT 884
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a method of increasing adenoviral gene expression in a tissue of an animal, comprising the step of administering to said animal a pharmacologically effective dose of tumor necrosis factor binding protein. Also provided is a various method of method of reducing an inflammatory response associated with adenoviral administration in a tissue of an animal, comprising the step of administering to said animal a pharmacologically effective dose of tumor necrosis factor binding protein.

L3 ANSWER 3 OF 59 USPATFULL
AN 2001:163320 USPATFULL
TI Anti-interleukin-1 receptor antagonist antibodies and uses thereof

IN Ford, John, San Mateo, CA, United States
Pace, Ann, Scotts Valley, CA, United States
PA Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI US 6294655 B1 20010925
AI US 1999-417455 19991013 (9)
RLI Continuation-in-part of Ser. No. US 1999-348942, filed on 7 Jul 1999 Continuation of Ser. No. US 1999-287210, filed on 5 Apr 1999, now abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on 17 Feb 1999, now abandoned Continuation-in-part of Ser. No. US 1998-127698, filed on 31 Jul 1998, now abandoned Continuation-in-part of Ser. No. US 1999-229591, filed on 13 Jan 1999, now abandoned Continuation of Ser. No. US 1998-99818, filed on 19 Jun 1998, now abandoned , said Ser. No. US 127698 Continuation-in-part of Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned , said Ser. No. US 99818 Continuation-in-part of Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-79909, filed on 15 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-55010, filed on 3 Apr 1998, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Spector, Lorraine
LREP Marshall, O'Toole Gerstein, Murray & Borun
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 4656
AB The present invention provides novel nucleic acids, the novel polypeptide sequences encoded by these nucleic acids and uses thereof. These novel polynucleotide and polypeptide sequences were determined to be a novel Interleukin-1 Receptor Antagonist. Also provided are antibodies which bind the antagonist, methods of detecting the antagonist, and kits containing the antibodies.

L3 ANSWER 4 OF 59 USPATFULL
AN 2001:152960 USPATFULL
TI Substituted 4-biarylbutyric and 5-biarylpentanoic acid derivatives as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene, Trumbull, CT, United States
Brittelli, David Ross, Branford, CT, United States
Schoen, William Riley, Madison, CT, United States
Ha, Sookhee Nicole, Woodbridge, CT, United States
PA Bayer Corporation, Pittsburgh, PA, United States (U.S. corporation)
PI US 6288063 B1 20010911
AI US 1998-85909 19980527 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2207
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Inhibitors for matrix metalloproteases, pharmaceutical compositions containing them, and a process for using them to treat a variety of

physiological conditions. The compounds of the invention have the generalized formula

(T).sub.x A--B--D--E--G

wherein A is an aryl or heteroaryl rings; B is an aryl or heteroaryl ring or a bond; each T is a substituent group; x is 0, 1, or 2; the group D represents ##STR1##

the group E represents a two or three carbon chain bearing one to three substituent groups which are independent or are involved in ring formation, possible structures being shown in the text and claims; and the group G represents ##STR2##

and with the proviso that when G is ##STR3##

each of the substituents on E is an independent substituent; and include pharmaceutically acceptable salts thereof.

L3 ANSWER 5 OF 59 USPATFULL
AN 2001:141891 USPATFULL
TI Use of mCRP to enhance immune responses
IN Potempa, Lawrence A., Deerfield, IL, United States
Radosevich, James A., Rockford, IL, United States
PA Immtech International, Inc., Vernon Hills, IL, United States (U.S. corporation)
PI US 6280743 B1 20010828
AI US 2000-568212 20000509 (9)
RLI Division of Ser. No. US 1999-376628, filed on 18 Aug 1999, now patented, Pat. No. US 6190670
PRAI US 1999-128888 19990412 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Saunders, David; Assistant Examiner: DeCloux, Amy
LREP Sheridan Ross P.C.
CLMN Number of Claims: 7
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 894
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a method of enhancing an immune response to an immunogen in an animal. The method comprises administering to the animal an effective amount of the immunogen and an effective amount of a modified C-reactive protein (mCRP) or a mutant-mCRP. The invention also provides a ***vaccine*** and a method of producing this ***vaccine*** . The ***vaccine*** comprises an immunogen and an mCRP or a mutant-mCRP in a pharmaceutically-acceptable vehicle. The invention further provides a kit for immunizing an animal to an immunogen comprising (1) a container holding the immunogen and a container holding an mCRP or a mutant-mCRP or (2) a container holding the immunogen and an mCRP or a mutant-mCRP. The invention also provides a method of elicing an immune response to a hapten in an animal. The method comprises administering to the animal an effective amount of the hapten in association with an an effective amount of an mCRP or a

mutant-mCRP. The invention further provides a ***vaccine*** and a method of producing this ***vaccine*** . The ***vaccine*** comprises a hapten and an mCRP or a mutant-mCRP in a pharmaceutically-acceptable vehicle. Finally, the invention provides a kit for immunizing an animal to a hapten comprising a container holding the hapten and an mCRP or a mutant-mCRP.

L3 ANSWER 6 OF 59 USPATFULL
AN 2001:136190 USPATFULL
TI Hemoglobin receptors from neisseriae
IN Stojiljkovic, Igor, Portland, OR, United States
So, Magdalene, Portland, OR, United States
Hwa, Vivian, Portland, OR, United States
Heffron, Fred, West Linn, OR, United States
Nassif, Xavier, Paris, France
PA Oregon Health Sciences University, Portland, OR, United States (U.S. corporation)
PI US 6277382 B1 20010821
WO 9612020 19960425
AI US 1997-817707 19970819 (8)
WO 1995-US13623 19951017
19970819 PCT 371 date
19970819 PCT 102(e) date
DT Utility
FS GRANTED
EXNAM Primary Examiner: Graser, Jennifer
LREP McDonnell Boehnen Hulbert & Berghoff
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 47 Drawing Page(s)
LN.CNT 1750
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel bacterial hemoglobin receptor proteins and genes that encode such proteins. The invention is directed toward the isolation, characterization, diagnostic and therapeutic use of bacterial hemoglobin receptor proteins, nucleic acids encoding such proteins, recombinant expression constructs comprising such nucleic acids and cells transformed therewith, and antibodies and epitopes of such hemoglobin receptor proteins. The invention relates particularly to hemoglobin receptor proteins and genes encoding such proteins from Neisseria species, especially N. meningitidis and serotypes thereof, and N. gonorrhoeae. Methods for the diagnostic and therapeutic use of the proteins, epitopes, antibodies and nucleic acids of the invention are also provided, including the use of proteins, epitopes, antibodies and nucleic acids of the invention for the production of ***vaccines*** effective in providing immunization of human against infection by pathogenic bacteria of Neisseria species.

L3 ANSWER 7 OF 59 USPATFULL
AN 2001:117039 USPATFULL
TI Pyrrolidine modulators of chemokine receptor activity
IN Caldwell, Charles, Scotch Plains, NJ, United States
Chapman, Kevin T., Scotch Plains, NJ, United States
Hale, Jeffrey, Westfield, NJ, United States

Kim, Dooseop, Westfield, NJ, United States
Lynch, Christopher, Scotch Plains, NJ, United States
MacCoss, Malcolm, Freehold, NJ, United States
Mills, Sander G., Scotch Plains, NJ, United States
Rosauer, Keith, Matawan, NJ, United States
Willoughby, Christopher, Edison, NJ, United States
Berk, Scott, Maplewood, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6265434 B1 20010724
AI US 2000-543024 20000404 (9)
PRAI US 1999-128035 19990406 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Patel, Sudhaker B.
LREP Walton, Kenneth R., Winokur, Melvin
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 8546
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to pyrrolidine compounds of the formula 1: ##STR1##

(wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6 and n are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3.

L3 ANSWER 8 OF 59 USPATFULL
AN 2001:102799 USPATFULL
TI Gene delivery by secretory gland expression
IN German, Michael, San Francisco, CA, United States
Goldfine, Ira D., Kentfield, CA, United States
Rothman, Stephen S., Berkeley, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 6255289 B1 20010703
AI US 1998-130886 19980807 (9)
RLI Continuation of Ser. No. US 1996-591197, filed on 16 Jan 1996, now patented, Pat. No. US 5885971 Continuation-in-part of Ser. No. US 1995-410660, filed on 24 Mar 1995, now patented, Pat. No. US 5837693
DT Utility
FS GRANTED
EXNAM Primary Examiner: Nguyen, Dave Trong
LREP Francis, Carol L., Borden, Paula A.Bozicevic, Field & Francis, LLP
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1670
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Secretory gland cells, particularly pancreatic and salivary gland cells, are genetically altered to operatively incorporate a gene which expresses a protein which has a desired therapeutic effect on a

mammalian subject. The expressed protein is secreted directly into the gastrointestinal tract and/or blood stream to obtain therapeutic blood levels of the protein thereby treating the patient in need of the protein. The transformed secretory gland cells provide long term therapeutic cures for diseases associated with a deficiency in a particular protein or which are amenable to treatment by overexpression of a protein.

L3 ANSWER 9 OF 59 USPATFULL
AN 2001:93521 USPATFULL
TI Pyrrolidine modulators of chemokine receptor activity
IN Chapman, Kevin, Scotch Plains, NJ, United States
Hale, Jeffrey, Westfield, NJ, United States
Kim, Dooseop, Westfield, NJ, United States
Lynch, Christopher, Scotch Plains, NJ, United States
Shah, Shrenik, Metuchen, NJ, United States
Shankaran, Kothandaraman, Kendall Park, NJ, United States
Shen, Dong-Ming, Edison, NJ, United States
Willoughby, Christopher, Clark, NJ, United States
MacCoss, Malcolm, Freehold, NJ, United States
Mills, Sander G., Scotch Plains, NJ, United States
Loebach, Jennifer L., Westfield, NJ, United States
Guthikonda, Ravindra N., Edison, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6248755 B1 20010619
AI US 2000-542617 20000404 (9)
PRAI US 1999-128033 19990406 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Seaman, D. Margaret
LREP Walton, Kenneth R., Winokur, Melvin
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 9773
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to pyrrolidine compounds of the formula I: ##STR1##

(wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6, R.sup.14 and n are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3.

L3 ANSWER 10 OF 59 USPATFULL
AN 2001:36840 USPATFULL
TI Heterosubstituted pyridine derivatives as PDE4 inhibitors
IN Cote, Bernard, L'ille Perrot, Canada
Friesen, Richard, Kirkland, Canada
Frenette, Richard, Laval, Canada
Girard, Mario, Ile Bizard, Canada
Girard, Yves, L'ille Bizard, Canada
Godbout, Cedrickx, Sherbrooke, Canada
Guay, Daniel, L'ille Perrot, Canada

Hamel, Pierre, Vimont-Laval, Canada
Blouin, Marc, St. Lazare-de-Vaudreuil, Canada
Ducharme, Yves, Montreal, Canada
Prescott, Sylvie, Chomedey, Canada
PA Merck Frosst Canada & Co., Kirkland, Canada (non-U.S. corporation)
PI US 6200993 B1 20010313
AI US 2000-551040 20000417 (9)
PRAI US 1999-132532 19990505 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Davis, Zinna Northington
LREP Lee, Shu M., Rose, David L.
CLMN Number of Claims: 19
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4209
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I useful in the treatment of diseases, including asthma, by raising the level of cyclic adenosine-3',5'-monophosphate (cAMP) through the inhibition of phosphodiesterase IV (PDE 4). ##STR1##

or a pharmaceutically acceptable salt or hydrate thereof.

The invention also encompasses pharmaceutical compositions and methods for treatment.

L3 ANSWER 11 OF 59 USPATFULL
AN 2001:25437 USPATFULL
TI Use of mCRP to enhance immune responses
IN Potempa, Lawrence A., Deerfield, IL, United States
Radosevich, James A., Rockford, IL, United States
PA Immtech International Inc., Vernon Hills, IL, United States (U.S. corporation)
PI US 6190670 B1 20010220
AI US 1999-376628 19990818 (9)
PRAI US 1999-128888 19990412 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Saunders, David; Assistant Examiner: DeCloux, Amy
LREP Sheridan Ross P.C.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 861
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a method of enhancing an immune response to an immunogen in an animal. The method comprises administering to the animal an effective amount of the immunogen and an effective amount of a modified C-reactive protein (mCRP) or a mutant-mCRP. The invention also provides a ***vaccine*** and a method of producing this ***vaccine*** . The ***vaccine*** comprises an immunogen and an mCRP or a mutant-mCRP in a pharmaceutically-acceptable vehicle. The invention further provides a kit for immunizing an animal to an

immunogen comprising (1) a container holding the immunogen and a container holding an mCRP or a mutant-mCRP or (2) a container holding the immunogen and an mCRP or a mutant-mCRP. The invention also provides a method of elicing an immune response to a hapten in an animal. The method comprises administering to the animal an effective amount of the hapten in association with an an effective amount of an mCRP or a mutant-mCRP. The invention further provides a ***vaccine*** and a method of producing this ***vaccine*** . The ***vaccine*** comprises a hapten and an mCRP or a mutant-mCRP in a pharmaceutically-acceptable vehicle. Finally, the invention provides a kit for immunizing an animal to a hapten comprising a container holding the hapten and an mCRP or a mutant-mCRP.

L3 ANSWER 12 OF 59 USPATFULL
AN 2001:4261 USPATFULL
TI Antibody formulation
IN Lam, Xanthe M., San Francisco, CA, United States
Oeswein, James Q., Moss Beach, CA, United States
Ongpipattanakul, Boonsri, Bangkok, Thailand
Shahrokh, Zahra, San Francisco, CA, United States
Wang, Sharon X., San Mateo, CA, United States
Weissburg, Robert P., Greenville, DE, United States
Wong, Rita L., San Mateo, CA, United States
PA Genentech, Inc., South San Francisco, CA, United States (U.S. corporation)
PI US 6171586 B1 20010109
AI US 1998-97171 19980612 (9)
PRAI US 1997-53087 19970613 (60)
DT Patent
FS Granted
EXNAM Primary Examiner: Nolan, Patrick; Assistant Examiner: DiBrino, Marianne
LREP Tan, Lee K., Lee, Wendy M.
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 38 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 2691
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A stable aqueous pharmaceutical formulation comprising a therapeutically effective amount of an antibody not subjected to prior lyophilization, a buffer maintaining the pH in the range from about 4.5 to about 6.0, a surfactant and a polyol is described, along with uses for such a formulation.

L3 ANSWER 13 OF 59 USPATFULL
AN 2000:174663 USPATFULL
TI Pyrrolidine and piperidine modulators of chemokine receptor activity
IN Budhu, Richard J., Monmouth Junction, NJ, United States
Holson, Edward, New York, NY, United States
Hale, Jeffrey J., Westfield, NJ, United States
Lynch, Christopher, Scotch Plains, NJ, United States
Maccoss, Malcolm, Freehold, NJ, United States
Berk, Scott C., Maplewood, NJ, United States
Mills, Sander G., Scotch Plains, NJ, United States
Willoughby, Christopher A., Clark, NJ, United States

PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6166037 20001226
AI US 1998-141227 19980827 (9)
PRAI US 1997-57743 19970828 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Chang, Ceila
LREP Thies, J. Eric, Rose, David L.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4273
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to pyrrolidine and piperidine compounds of the formula I: ##STR1## (wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4a, R.sup.4b, R.sup.4c, R.sup.4d, R.sup.4e, R.sup.4f, R.sup.4g, R.sup.4h, m, n, x and y are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4.

L3 ANSWER 14 OF 59 USPATFULL
AN 2000:142393 USPATFULL
TI Cyclic amine modulations of chemokine receptor activity
IN Caldwell, Charles G., Scotch Plains, NJ, United States
Finke, Paul E., Milltown, NJ, United States
Maccoss, Malcolm, Freehold, NJ, United States
Meurer, Laura C., Scotch Plains, NJ, United States
Mills, Sander G., Scotch Plains, NJ, United States
Oates, Bryan, Wayne, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6136827 20001024
AI US 1998-120010 19980721 (9)
PRAI US 1997-53754 19970725 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Chang, Ceila
LREP Thies, J. Eric, Rose, David L.
CLMN Number of Claims: 20
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3161
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to cyclic amines of the formula I: ##STR1## (wherein R.sup.1, R.sup.2, R.sup.3, m and n are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4.

L3 ANSWER 15 OF 59 USPATFULL
AN 2000:124815 USPATFULL
TI Bacterial hemoglobin receptor genes
IN Stojiljkovic, Igor, 3223 SW. 11th Ave. #3, Portland, OR, United States

97201
So, Magdalene, 777 SW. 48th Dr., Portland, OR, United States 97221
Hwa, Vivian, 7011 SW. 4th Ave., Portland, OR, United States 97219
Heffron, Fred, 17887 Hillside Dr., West Linn, OR, United States 97068
Nassif, Xavier, 36 Rue Miollis, Paris, France
PI US 6121037 20000919
AI US 1995-537361 19951002 (8)
RLI Continuation-in-part of Ser. No. US 1994-326670, filed on 18 Oct 1994, now patented, Pat. No. US 5698438
DT Utility
FS Granted
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Hayes, Robert C.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 47 Drawing Figure(s); 47 Drawing Page(s)
LN.CNT 3180
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel bacterial hemoglobin receptor proteins and genes that encode such proteins. The invention is directed toward the isolation, characterization, diagnostic and therapeutic use of bacterial hemoglobin receptor proteins, nucleic acid encoding such proteins, recombinant expression constructs comprising such nucleic acids and cells transformed therewith, and antibodies and epitopes of such hemoglobin receptor proteins. The invention relates particularly to hemoglobin receptor proteins and genes encoding such proteins from Neisseria species, especially N. meningitidis and serotypes thereof, and N. gonorrhoeae. Methods for the diagnostic and therapeutic use of the proteins, epitopes, antibodies and nucleic acids of the invention are also provided, including the use of the proteins, epitopes, antibodies and nucleic acids of the invention for the production of ***vaccines*** effective in providing immunization of a human against infection by pathogenic bacteria of Neisseria species.

L3 ANSWER 16 OF 59 USPATFULL
AN 2000:87707 USPATFULL
TI Methods and compositions for the inhibition of interleukin-12 production
IN Karp, Christopher L., Lutherville, MD, United States
Trinchieri, Giorgio, Wynnewood, PA, United States
Wysocka, Maria, Wynnewood, PA, United States
Griffin, Diane E., Hunt Valley, MD, United States
PA The Wistar Insitute, Philadelphia, PA, United States (U.S. corporation)
Johns Hopkins University, Baltimore, MD, United States (U.S. corporation)
PI US 6086876 20000711
AI US 1998-19862 19980206 (9)
PRAI US 1997-37722 19970207 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Kemmerer, Elizabeth; Assistant Examiner: Romeo, David S.
LREP Akin, Gump, Strauss, Hauer & Feld, L.L.P.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1

DRWN 13 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 1487
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention includes compositions and methods for selective suppression of IL-12 production in a cell. Methods of treating a human having a disease associated with dysregulated IL-12 production are also provided.

L3 ANSWER 17 OF 59 USPATFULL
AN 2000:80798 USPATFULL
TI Tri-substituted phenyl derivatives and processes for their preparations
IN Boyd, Ewan Campbell, Slough, United Kingdom
Eaton, Michael Anthony William, Watlington, United Kingdom
Warrellow, Graham John, Northwood, United Kingdom
PA Celltech Therapeutics, Limited, United Kingdom (non-U.S. corporation)
PI US 6080790 20000627
AI US 1997-862942 19970530 (8)
RLI Division of Ser. No. US 1995-465871, filed on 6 Jun 1995, now patented, Pat. No. US 5674880 which is a division of Ser. No. US 1995-387551, filed on 13 Feb 1995, now patented, Pat. No. US 5491147 which is a continuation of Ser. No. US 1993-141873, filed on 22 Oct 1993, now abandoned
PRAI GB 1992-22253 19921023
DT Utility
FS Granted
EXNAM Primary Examiner: Lambkin, Deborah C.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1523
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (1) ##STR1## are described wherein Y represents a halogen atom or a group --OR.sup.1, where R.sup.1 is an optionally substituted alkyl group; R.sup.2 represents an optionally substituted cycloalkyl or cycloalkenyl group; R.sup.3 is a monocyclic or bicyclic aryl group optionally containing one or more heteroatoms selected from oxygen or sulphur atoms or a group --N(R.sup.4)-- where R.sup.4 is a hydrogen atom or an alkyl group; X is --O--, --S--, or --N(R.sup.5)--, where R.sup.5 is a hydrogen or an alkyl group; with the proviso that when X is --O-- then R.sup.3 is not a 3-cyanamino-6-pyridazinyl or a 3-chloro-6-pyridazinyl group; and the salts, solvates, hydrates and N-oxides thereof.

The compounds are selective and potent inhibitors of phosphodiesterase IV and are useful for the prophylaxis and treatment of inflammatory diseases and the alleviation of conditions associated with central nervous malfunction.

L3 ANSWER 18 OF 59 USPATFULL
AN 2000:80415 USPATFULL
TI Diagnostic assays for MIF
IN Bucala, Richard J., New York, NY, United States
Mitchell, Robert A., New York, NY, United States

Bernhagen, Jurgen, New York, NY, United States
Calandra, Thierry F., New York, NY, United States
Cerami, Anthony, Shelter Island, NY, United States
PA The Picower Institute for Medical Research, Manhasset, NY, United States (U.S. corporation)
PI US 6080407 20000627
AI US 1995-471586 19950606 (8)
RLI Division of Ser. No. US 1995-462350, filed on 5 Jun 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-243342, filed on 16 May 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-63399, filed on 17 May 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Chan, Christina Y.; Assistant Examiner: Nolan, Patrick
LREP Oster, Jeffrey B.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 26 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 3585
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to compositions and methods for inhibiting the release and/or biological activity of migration inhibitory factor (MIF). In particular, the invention relates to the uses of such compositions and methods for the treatment of various conditions involving cytokine-mediated toxicity, which include, but are not limited to shock, inflammation, graft versus host disease, and/or autoimmune diseases.

L3 ANSWER 19 OF 59 USPATFULL
AN 2000:24289 USPATFULL
TI Combination method for treating diseases caused by cytokine-mediated toxicity
IN Bucala, Richard J., New York, NY, United States
Mitchell, Robert A., New York, NY, United States
Bernhagen, Jurgen, New York, NY, United States
Calandra, Thierry F., New York, NY, United States
Cerami, Anthony, Shelter Island, NY, United States
PA The Picower Institute for Medical Research, Manhasset, NY, United States (U.S. corporation)
PI US 6030615 20000229
AI US 1995-471546 19950606 (8)
RLI Division of Ser. No. US 1995-462350, filed on 5 Jun 1995 which is a continuation-in-part of Ser. No. US 1994-243342, filed on 16 May 1994 which is a continuation-in-part of Ser. No. US 1993-63399, filed on 17 May 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Bansal, Geetha P.
LREP Tremaine, Davis Wright
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 28 Drawing Figure(s); 22 Drawing Page(s)
LN.CNT 3534

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB There is disclosed a method for treating an individual having a disease caused by cytokine-mediated toxicity comprising administering to the individual an effective amount of (a) an antibody that binds to an MIF polypeptide, wherein the MIF polypeptide has a molecular weight of about 12.5 kDa in combination with (b) anti-TNF.alpha., anti-IL1, anti-IFN-.gamma., IL-1RA, a steroid, a glucocorticoid, or IL-10.

L3 ANSWER 20 OF 59 USPATFULL

AN 2000:21663 USPATFULL

TI Chemokine .beta.-6 antagonists

IN Kreider, Brent L., Germantown, MD, United States
Ruben, Steven M., Olney, MD, United States
Olsen, Henrik S., Gaithersburg, MD, United States

PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)

PI US 6028169 20000222

AI US 1997-995156 19971219 (8)

PRAI US 1997-42269 19970331 (60)

DT Utility

FS Granted

EXNAM Primary Examiner: Kemmerer, Elizabeth

LREP Sterne, Kessler, Goldstein & Fox P.L.L.C.

CLMN Number of Claims: 129

ECL Exemplary Claim: 1

DRWN 34 Drawing Figure(s); 29 Drawing Page(s)

LN.CNT 5814

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Human chemokine .beta.-6 agonist and antagonist polypeptides and DNA encoding such polypeptides and procedure for producing such polypeptides by recombinant technique are disclosed. The chemokine .beta.-6 antagonists of the present invention may be employed to treat rheumatoid arthritis, lung inflammation, allergy, asmtha, infectious diseases and to prevent inflammation and atherosclerosis. The chemokine .beta.-6 agonists may be employed to myeloprotect patients undergoing chemotherapy.

L3 ANSWER 21 OF 59 USPATFULL

AN 1999:170435 USPATFULL

TI Interleukin-1 beta converting enzyme like apoptotic protease-7

IN Dixit, Vishva M., Ann Arbor, MI, United States
Kikly, Kristine K., Linfield, PA, United States
Ruben, Steven M., Olney, MD, United States
Ni, Jian, Rockville, MD, United States
Rosen, Craig A., Laytonsville, MD, United States

PA Smithkline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
The Regents of the University of Michigan, Ann Arbor, MI, United States (U.S. corporation)
Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)

PI US 6008042 19991228

AI US 1997-852782 19970507 (8)

PRAI US 1996-19365 19960605 (60)

US 1996-17454 19960517 (60)
US 1996-17914 19960516 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Campell, Bruce R.; Assistant Examiner: Nguyen, Dave Trong
LREP Han, William T.Ratner & Prestia, King, William T.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 9 Drawing Page(s)
LN.CNT 3044
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Human ICE LAP-7 polypeptides and DNA (RNA) encoding such ICE LAP-7 and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such ICE LAP-7 for the treatment of a susceptibility to viral infection, tumorogenesis and to diseases and defects in the control embryogenesis and tissue homeostasis, and the nucleic acid sequences described above may be employed in an assay for ascertaining such susceptibility. Antagonists against such ICE LAP-7 and their use as a therapeutic to treat Alzheimer's disease, Parkinson's disease, rheumatoid arthritis, septic shock, sepsis, stroke, chronic inflammation, acute inflammation, CNS inflammation, osteoporosis, ischemia reperfusion injury, cell death associated with cardiovascular disease, polycystic kidney disease, apoptosis of endothelial cells in cardiovascular disease, degenerative liver disease, MS, ALS, cererbellar degeneration, ischemic injury, myocardial infarction, AIDS, myelodysplastic syndromes, aplastic anemia, male pattern baldness, and head injury damage are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding the interleukin-1 beta converting enzyme apoptosis proteases and for detecting altered levels of the polypeptide in a host.

L3 ANSWER 22 OF 59 USPATFULL
AN 1999:166984 USPATFULL
TI Protein delivery by secretory gland expression
IN Rothman, Stephen S., Berkeley, CA, United States
Goldfine, Ira D., Kentfield, CA, United States
German, Michael S., San Francisco, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 6004944 19991221
AI US 1997-942939 19971002 (8)
RLI Continuation-in-part of Ser. No. US 1996-591197, filed on 16 Jan 1996, now patented, Pat. No. US 5885971 which is a continuation-in-part of Ser. No. US 1995-410660, filed on 24 Mar 1995, now patented, Pat. No. US 5837693
DT Utility
FS Granted
EXNAM Primary Examiner: Priebe, Scott D.; Assistant Examiner: Nguyen, Dave Trong
LREP Francis, Carol L.Bozicevic, Field & Francis, LLP

CLMN Number of Claims: 31
ECL Exemplary Claim: 1
DRWN 24 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 1989
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Secretory gland cells, particularly pancreatic, hepatic, and salivary gland cells, are genetically altered to operatively incorporate a gene which expresses a protein which has a desired therapeutic effect on a mammalian subject. The expressed protein is secreted directly into the bloodstream to obtain therapeutic levels of the protein thereby treating the patient in need of the protein. The transformed secretory gland cells provide long term or short term therapies for diseases associated with a deficiency in a particular protein or which are amenable to treatment by overexpression of a protein.

L3 ANSWER 23 OF 59 USPATFULL
AN 1999:163462 USPATFULL
TI Polynucleotides encoding myeloid progenitor inhibitory factor-1 (MPIF-1) and polypeptides encoded thereby
IN Ruben, Steven M., Olney, MD, United States
Li, Haodong, Gaithersburg, MD, United States
PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
PI US 6001606 19991214
AI US 1996-722719 19960930 (8)
RLI Continuation-in-part of Ser. No. US 1995-446881, filed on 5 May 1995, now abandoned which is a continuation-in-part of Ser. No. US 1995-465682, filed on 6 Jun 1995, now abandoned which is a continuation-in-part of Ser. No. US 1994-208339, filed on 8 Mar 1994, now patented, Pat. No. US 5504003 Ser. No. Ser. No. US 1995-468775, filed on 6 Jun 1995, now abandoned And Ser. No. WO 1996-US15592, filed on 27 Sep 1996 , said Ser. No. US 465682 which is a continuation-in-part of Ser. No. US 446881 , said Ser. No. US 468775 which is a continuation-in-part of Ser. No. US 446881
PRAI US 1995-4517 19950929 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Mertz, Prema
LREP Sterne, Kessler, Goldstein & Fox, P.L.L.C.
CLMN Number of Claims: 74
ECL Exemplary Claim: 1
DRWN 53 Drawing Figure(s); 49 Drawing Page(s)
LN.CNT 6406
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB There are disclosed therapeutic compositions and methods using isolated nucleic acid molecules encoding a human myeloid progenitor inhibitory factor-1 (MPIF-1) polypeptide (previously termed MIP-3 and chemokine .beta.8(CK.beta.8 or ckb-8)); a human monocyte-colony inhibitory factor (M-CIF) polypeptide (previously termed MIP1-.gamma. and chemokine .beta.1(CK.beta.1 or ckb-1)), and a macrophage inhibitory protein-4 (MIP-4), as well as MPIF-1, M-CIF and/or MIP-4 polypeptides themselves, as are vectors, host cells and recombinant methods for producing the same.

L3 ANSWER 24 OF 59 USPATFULL
AN 1999:159997 USPATFULL
TI Compounds that bind bacterial pili
IN Shekhani, Mohammed Saleh, Madison, WI, United States
Firca, Joseph R., Vernon Hills, IL, United States
Anderson, Byron, Morton Grove, IL, United States
PA Ophidian Pharmaceuticals, Inc., Madison, WI, United States (U.S. corporation)
PI US 5998381 19991207
AI US 1996-760903 19961206 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Peselev, Elli
LREP Medlen & Carroll, LLP
CLMN Number of Claims: 24
ECL Exemplary Claim: 5
DRWN 23 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 6570
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Diagnostics and treatments for bacterial infection are disclosed. The treatments prevent bacteria from adhering to host cells by interfering with the binding of the bacteria to cell receptors. Compounds that inhibit bacterial adherence to cells are engineered to be readily modified for best efficacy with different modes of treatment. The compounds can be readily modified for use to identify bacteria according to their cell binding specificities.

L3 ANSWER 25 OF 59 USPATFULL
AN 1999:159484 USPATFULL
TI Method of using humanized antibody against CD18
IN Waldmann, Herman, 4 Apsley Road, Oxford, United Kingdom OX2 7QY
Sims, Martin J., 29 Hines Lane, Comberton, Cambridge, United Kingdom CB3 7BZ
Crowe, J. Scott, 25 Earlsmead, Letchworth, Herts. SG6 3UE, United Kingdom
PI US 5997867 19991207
AI US 1995-465313 19950605 (8)
RLI Continuation of Ser. No. US 1994-182067, filed on 23 Mar 1994
PRAI GB 1991-15364 19910716
DT Utility
FS Granted
EXNAM Primary Examiner: Chan, Christina Y.; Assistant Examiner: Gambel, Phillip
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1352
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treating patients suffering from, or at risk of developing, a leukocyte mediated disease comprising the administration of humanized antibodies and fragments thereof that bind human CD18 are disclosed.

L3 ANSWER 26 OF 59 USPATFULL

AN 1999:145979 USPATFULL
TI Humanized antibody against CD18
IN Waldmann, Herman, University of Cambridge, Department of Pathology Tennis Court Road, Cambridge, United Kingdom CB2 1QP
Sims, Martin, The Wellcome Foundation Limited Langley Court, Beckenham, United Kingdom
Crowe, Scott, The Wellcome Foundation Limited Langley Court, Beckenham, United Kingdom BR3 3BS
PI US 5985279 19991116
WO 9302191 19930204
AI US 1994-182067 19940323 (8)
WO 1992-GB1289 19920715
19940323 PCT 371 date
19940323 PCT 102(e) date
PRAI GB 1991-15364 19910716
DT Utility
FS Granted
EXNAM Primary Examiner: Chan, Christina Y.; Assistant Examiner: Gambel, Phillip
LREP Hamilton, Brook, Smith & Reynolds, P.C.
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1404
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Humanized antibodies and fragments thereof that bind human CD18 are disclosed. Nucleic acids encoding anti-CD18 antibodies or fragments thereof, as well as expression vectors and host cells incorporating these nucleic acids for the recombinant expression of anti-CD18 antibodies are also encompassed by the invention. Pharmaceutical compositions comprising the antibodies of the invention are also disclosed.

L3 ANSWER 27 OF 59 USPATFULL
AN 1999:121364 USPATFULL
TI Spiro-substituted azacycles as modulators of chemokine receptor activity
IN Mills, Sander G., Scotch Plains, NJ, United States
Maccoss, Malcolm, Freehold, NJ, United States
Springer, Martin S., Westfield, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 5962462 19991005
AI US 1997-989947 19971212 (8)
PRAI US 1996-32735 19961213 (60)
US 1996-33558 19961220 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Oazi, Sabiha N.
LREP Thies, J. Eric, Rose, David L.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 6786
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to spiro-substituted azacycles of the

Formula 1: ##STR1## (wherein R.sub.1, l, m, Q, W, X, Y, and Z are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4.

L3 ANSWER 28 OF 59 USPATFULL
AN 1999:110187 USPATFULL
TI DNA encoding the chemotactic cytokine III
IN Ni, Jian, Rockville, MD, United States
Gentz, Reiner, Silver Spring, MD, United States
Yu, Guo-Liang, Darnestown, MD, United States
Su, Jeffrey, Gaithersburg, MD, United States
Dillon, Patrick J., Gaithersburg, MD, United States
PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
PI US 5952197 19990914
AI US 1997-812003 19970305 (8)
PRAI US 1996-13609 19960305 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Draper, Garnette D.
LREP Wales, Michele M.
CLMN Number of Claims: 28
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 2323
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Human chemotactic cytokine III polypeptides and DNA (RNA) encoding such chemotactic cytokines and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such chemotactic cytokines for the treatment of leukemia, tumors, chronic infections, auto-immune disease, fibrotic disorders, wound healing and psoriasis. Antagonists against such chemotactic cytokines and their use as a therapeutic to treat rheumatoid arthritis, auto-immune and chronic and acute inflammatory and infective diseases, allergic reactions, prostaglandin-independent fever, cerebral ischemia, glomerulonephritis, HTLV-1 related diseases and bone marrow failure are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding chemotactic cytokine III and for detecting altered levels of the polypeptide in a host.

L3 ANSWER 29 OF 59 USPATFULL
AN 1999:96476 USPATFULL
TI Methods of treating inflammation and compositions therefor
IN McFadden, D. Grant, Edmonton, Canada
Lucas, Alexandra, Edmonton, Canada
PA Viron Therapeutics, Inc., London, Canada (non-U.S. corporation)
PI US 5939525 19990817
AI US 1995-411043 19950327 (8)
DT Utility

FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Delaney, Patrick R.
LREP Scully, Scott, Murphy & Presser
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 23 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 2356
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods for treating inflammatory cell infiltration in a tissue of a mammalian subject are provided. The method involves administering a therapeutically effective amount of SERP-1, SERP-1 analog or biologically active fragment thereof admixed with a pharmaceutically acceptable carrier to a subject in need of such treatment. Biologically active SERP-1 analogs are also provided. The compositions and methods of the present invention are useful for treating numerous inflammatory based diseases and injuries.

L3 ANSWER 30 OF 59 USPATFULL
AN 1999:75756 USPATFULL
TI Modified hookworm neutrophil inhibitors
IN Moyle, Matthew, Escondido, CA, United States
Foster, David L., Brighton, MA, United States
PA Corvas International, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5919900 19990706
AI US 1995-450497 19950526 (8)
RLI Division of Ser. No. US 1993-173510, filed on 23 Dec 1993 which is a continuation-in-part of Ser. No. US 1993-151064, filed on 10 Nov 1993 which is a continuation-in-part of Ser. No. US 1993-60433, filed on 11 May 1993 which is a continuation-in-part of Ser. No. US 1992-996972, filed on 24 Dec 1992 which is a continuation-in-part of Ser. No. US 1992-881721, filed on 11 May 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Fitzgerald, David L.; Assistant Examiner: Lathrop, Brian
LREP Lyon & Lyon LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 69 Drawing Figure(s); 56 Drawing Page(s)
LN.CNT 5740
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions enriched for Neutrophil Inhibitory Factor which inhibit neutrophil activity including adhesion to vascular endothelial cells are provided. Also provided are recombinant Neutrophil Inhibitory Factors which also which inhibit neutrophil activity. Such compositions may comprise a glycoprotein isolated from nematodes. These compositions and recombinant Neutrophil Inhibitory Factors are useful in the therapy of conditions which involve abnormal or undesired inflammatory responses.

L3 ANSWER 31 OF 59 USPATFULL
AN 1999:72706 USPATFULL
TI Methods of treating inflammation and compositions therefor

IN McFadden, D. Grant, Edmonton, Canada
Lucas, Alexandra, Edmonton, Canada
PA Viron Therapeutics, Inc., London, Canada (non-U.S. corporation)
PI US 5917014 19990629
AI US 1995-468865 19950606 (8)
RLI Continuation of Ser. No. US 1995-411043, filed on 27 Mar 1995
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Delaney, Patrick R.
LREP Scully, Scott, Murphy & Presser
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 23 Drawing Figure(s); 15 Drawing Page(s)
LN.CNT 2074
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods for treating inflammatory cell infiltration in a tissue of a mammalian subject are provided. The method involves administering a therapeutically effective amount of SERP-1, SERP-1 analog or biologically active fragment thereof admixed with a pharmaceutically acceptable carrier to a subject in need of such treatment. Biologically active SERP-1 analogs are also provided. The compositions and methods of the present invention are useful for treating numerous inflammatory based diseases and injuries.

L3 ANSWER 32 OF 59 USPATFULL
AN 1999:65188 USPATFULL
TI Polynucleotides encoding chemokine .alpha.-2
IN Ni, Jian, Rockville, MD, United States
Gentz, Reiner L., Silver Spring, MD, United States
Su, Jeffrey Y., Gaithersburg, MD, United States
Li, Haodong, Gaithersburg, MD, United States
PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
PI US 5910431 19990608
AI US 1997-825556 19970319 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Draper, Garnette D.
LREP Sterne, Kessler, Goldstein & Fox P.L.L.C.
CLMN Number of Claims: 26
ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 2491
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Human chemokine Alpha-2 polypeptides and DNA (RNA) encoding such chemotactic cytokines and a procedure for producing such polypeptides by recombinant techniques is disclosed. Also disclosed are methods for utilizing such chemotactic cytokines for the treatment of leukemia, tumors, chronic infections, auto-immune disease, fibrotic disorders, wound healing and psoriasis. Antagonists against such chemotactic cytokines and their use as a therapeutic to treat rheumatoid arthritis, autoimmune and chronic and acute inflammatory and infective diseases, allergic reactions, prostaglandin-independent fever and bone marrow

failure are also disclosed. Also disclosed are diagnostic assays for detecting diseases related to mutations in the nucleic acid sequences and altered concentrations of the polypeptides. Also disclosed are diagnostic assays for detecting mutations in the polynucleotides encoding the chemotactic cytokines and for detecting altered levels of the polypeptides in a host.

L3 ANSWER 33 OF 59 USPATFULL
AN 1999:37087 USPATFULL
TI Gene therapy by secretory gland expression
IN German, Michael, San Francisco, CA, United States
Goldfine, Ira D., Kentfield, CA, United States
Rothman, Stephen S., Berkeley, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 5885971 19990323
AI US 1996-591197 19960116 (8)
RLI Continuation-in-part of Ser. No. US 1995-410660, filed on 24 Mar 1995
DT Utility
FS Granted
EXNAM Primary Examiner: Campell, Bruce R.
LREP Francis, Carol L.Bozicevic & Reed LLP
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 10 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 1680
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Secretory gland cells, particularly pancreatic and salivary gland cells, are genetically altered to operatively incorporate a gene which expresses a protein which has a desired therapeutic effect on a mammalian subject. The expressed protein is secreted directly into the gastrointestinal tract and/or blood stream to obtain therapeutic blood levels of the protein thereby treating the patient in need of the protein. The transformed secretory gland cells provide long term therapeutic cures for diseases associated with a deficiency in a particular protein or which are amenable to treatment by overexpression of a protein.

L3 ANSWER 34 OF 59 USPATFULL
AN 1999:24463 USPATFULL
TI Mutant protein and methods and materials for making and using it
IN Potempa, Lawrence A., Deerfield, IL, United States
Liao, Hans H., Oakville, Canada
Crump, Becky L., Evanston, IL, United States
PA Immtech International Inc., Evanston, IL, United States (U.S. corporation)
PI US 5874238 19990223
AI US 1995-480270 19950607 (8)
RLI Division of Ser. No. US 1994-296545, filed on 26 Aug 1994, now abandoned which is a continuation-in-part of Ser. No. US 1993-23952, filed on 26 Feb 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Patterson, Jr., Charles L.

LREP Brinks Hofer Gilson & Lione
CLMN Number of Claims: 18
ECL Exemplary Claim: 1
DRWN 33 Drawing Figure(s); 24 Drawing Page(s)
LN.CNT 2937
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention provides a mutant protein which has the same amino acid sequence as an unmutated C-reactive protein (CRP) subunit or an unmutated preCRP, except that at least one amino acid of the unmutated CRP subunit or unmutated preCRP has been deleted, at least one amino acid of the unmutated CRP subunit or unmutated preCRP has been replaced by another amino acid, at least one amino acid has been added to the unmutated CRP subunit or preCRP, or a combination of such changes has been made. The amino acid(s) added, deleted and/or replaced are chosen so that the mutant protein is less likely to form covalently cross-linked aggregates than the unmutated CRP subunit or unmutated preCRP. The mutant protein also exhibits at least one of the biological activities of modified-CRP. The invention also provides DNA molecules coding for the mutant proteins of the invention, vectors for expressing the mutant proteins, host cells which have been transformed so that they can express the mutant proteins, and a method of producing the mutant proteins of the invention comprising culturing the transformed host cells. Finally, the invention provides methods and materials for using the mutant proteins.

L3 ANSWER 35 OF 59 MEDLINE
AN 1999256450 MEDLINE
DN 99256450 PubMed ID: 10323074
TI [A new possibility for enhancing natural immunity: a radiation-detoxified endotoxin].
A termeszetes ellenallokepesseg fokozasanak uj lehetosege: a sugarzassal meregtelenitett endotoxin.
AU Bertok L
CS OKK, Orszagos Frederic Joliot Curie Sugarbiologiai es Sugaregeszsegugyi Kutato Intezet, Budapest.
SO ORVOSI HETILAP, (1999 Apr 11) 140 (15) 819-27. Ref: 50
Journal code: OL8; 0376412. ISSN: 0030-6002.
CY Hungary
DT Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW LITERATURE)
LA Hungarian
FS Priority Journals
EM 199905
ED Entered STN: 19990601
Last Updated on STN: 19990601
Entered Medline: 19990520
AB Using ionizing radiation the author and co-workers produced a detoxified endotoxin preparation (Tolerin) which seems to be a suitable product for the increase of natural immunity (nonspecific resistance)-including activation of bone marrow in immunosuppressions, immunodeficiencies-protection against various types of shocks-radiation injury, septic/ ***endotoxic*** ***shock*** , etc.- and increase of immunogen effect of antigens (e.g. inactivated virus ***vaccines***) as an

immunoadjuvant in human beings and experimental animals.

L3 ANSWER 36 OF 59 USPATFULL
AN 1998:115714 USPATFULL
TI Pharmaceutical dipeptide compositions and methods of use thereof: immunodepressants
IN Khavinson, Vladimir Kh., St. Petersburg, Russian Federation
Morozov, Vyacheslav G., St. Petersburg, Russian Federation
PA Cytran, Inc., Kirkland, WA, United States (U.S. corporation)
PI US 5811399 19980922
AI US 4509048 19950526 (8)
RLI Continuation-in-part of Ser. No. 278463, filed on 21 Jul 1994, now abandoned And Ser. No. 337341, filed on 10 Nov 1994, now patented, Pat. No. 5538951 which is a continuation-in-part of Ser. No. 257495, filed on 7 Jun 1994, now abandoned which is a continuation of Ser. No. 783518, filed on 28 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. 678129, filed on 1 Apr 1991, now abandoned which is a continuation-in-part of Ser. No. 415283, filed on 30 Aug 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Tsang, Cecilia J.; Assistant Examiner: Harle, Jennifer
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 8863
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treatment of subjects for decreasing cell mediated autoimmunity or humoral autoimmunity by administering an R'-Glu-Trp-R" pharmaceutical preparation useful in subjects having autoimmune diseases.

L3 ANSWER 37 OF 59 USPATFULL
AN 1998:144092 USPATFULL
TI Intravenous hormone polypeptide delivery by salivary gland expression
IN German, Michael, San Francisco, CA, United States
Goldfine, Ira D., Kentfield, CA, United States
Rothman, Stephen S., Berkeley, CA, United States
PA The Regents of the University of California, Oakland, CA, United States (U.S. corporation)
PI US 5837693 19981117
AI US 1995-410660 19950324 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Low, Christopher S. F.; Assistant Examiner: Nguyen, Dave Trong
LREP Francis, Carol L.Bozicevic & Reed LLP
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 4 Drawing Figure(s); 4 Drawing Page(s)
LN.CNT 1540
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Secretory gland cells, particularly pancreatic and salivary gland cells, are genetically altered to operatively incorporate a gene which

expresses a protein which has a desired therapeutic effect on a mammalian subject. The expressed protein is secreted directly into the gastrointestinal tract and/or blood stream to obtain therapeutic blood levels of the protein thereby treating the patient in need of the protein. The transformed secretory gland cells provide long term therapeutic cures for diseases associated with a deficiency in a particular protein or which are amenable to treatment by overexpression of a protein.

L3 ANSWER 38 OF 59 USPATFULL
AN 1998:138436 USPATFULL
TI Composition and method for preventing and treating inflammation with Immunoglobulin A
IN Eibl, Martha, Vienna, Austria
Wolf, Hermann, Vienna, Austria
Mannhalter, Josef W., Vienna, Austria
Leibl, Heinz, Vienna, Austria
Linnau, Yendra, Vienna, Austria
PA Immuno Aktiengesellschaft, Vienna, Austria (non-U.S. corporation)
PI US 5833984 19981110
AI US 1996-772264 19961223 (8)
RLI Continuation of Ser. No. US 1994-198067, filed on 18 Feb 1994, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Eisenschenk, Frank C.
LREP Foley & Lardner
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 975
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Inflammation can be treated or prevented altogether by administering a preparation comprising IgA. These preparations also can effect immunomodulation. Preferably, the preparation includes multimeric IgA and is essentially free of IgG in its various forms. Other compounds, such as antibiotics, antiphlogistic agents and antacids, also may be administered. Immunoglobulin A may also be used in ***vaccines*** to prevent inflammation. Additionally, an improved assay for evaluating anti-inflammatory activity is provided.

L3 ANSWER 39 OF 59 USPATFULL
AN 1998:111911 USPATFULL
TI Method for treatment of purulent inflammatory diseases
IN Morozov, Vyacheslav G., St. Petersburg, Russian Federation
Khavinson, Vladimir Kh., St. Petersburg, Russian Federation
PA Cytoven J.V., Kirkland, WA, United States (U.S. corporation)
PI US 5807830 19980915
AI US 1995-452061 19950526 (8)
RLI Continuation-in-part of Ser. No. US 1994-337341, filed on 10 Nov 1994, now patented, Pat. No. US 5538951 And a continuation-in-part of Ser. No. US 1994-278463, filed on 21 Jul 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-257495, filed on 7 Jun 1994, now abandoned which is a continuation of Ser. No. US 1991-783518, filed

on 28 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-678129, filed on 1 Apr 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-415283, filed on 30 Aug 1989, now abandoned
PRAI SU 1987-4352833 19871230
DT Utility
FS Granted
EXNAM Primary Examiner: Jones, W. Gary; Assistant Examiner: Fredman, Jeffrey
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 8879
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods of treating purulent inflammatory diseases by administering L-Glu-L-Trp or a salt thereof.

L3 ANSWER 40 OF 59 USPATFULL
AN 1998:91809 USPATFULL
TI Neutrophil inhibitors
IN Moyle, Matthew, Escondido, CA, United States
Foster, David L., Brighton, MA, United States
Vlasuk, George P., Carlsbad, CA, United States
PA Corvas International, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5789178 19980804
AI US 1995-458218 19950602 (8)
RLI Continuation of Ser. No. US 1993-151064, filed on 10 Nov 1993 which is a continuation-in-part of Ser. No. US 1993-60433, filed on 11 May 1993 which is a continuation-in-part of Ser. No. US 1992-996972, filed on 24 Dec 1992 which is a continuation-in-part of Ser. No. US 1992-881721, filed on 11 May 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Basham, Daryl A.
LREP Lyon & Lyon LLP
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 65 Drawing Figure(s); 56 Drawing Page(s)
LN.CNT 5374
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions enriched for Neutrophil Inhibitory Factor which inhibit neutrophil activity including adhesion to vascular endothelial cells are provided. Also provided are recombinant Neutrophil Inhibitory Factors which also which inhibit neutrophil activity. Such compositions may comprise a glycoprotein isolated from nematodes. These compositions and recombinant Neutrophil Inhibitory Factors are useful in the therapy of conditions which involve abnormal or undesired inflammatory responses.

L3 ANSWER 41 OF 59 USPATFULL
AN 1998:72601 USPATFULL
TI Pharmaceutical dipeptide compositions and methods of use thereof: systemic toxicity
IN Morozov, Vyacheslav G., St. Petersburg, Russian Federation
Khavinson, Vladimir Kh., St. Petersburg, Russian Federation

PA Cytran, Inc., Kirkland, WA, United States (U.S. corporation)
PI US 5770576 19980623
AI US 1995-452077 19950526 (8)
RLI Continuation of Ser. No. US 1994-337341, filed on 10 Nov 1994, now patented, Pat. No. US 5538951 which is a division of Ser. No. US 1989-415283, filed on 30 Aug 1989 And a continuation-in-part of Ser. No. US 1994-278463, filed on 21 Jul 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-257495, filed on 7 Jun 1994, now abandoned which is a continuation of Ser. No. US 1991-783518, filed on 28 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-678129, filed on 1 Apr 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-415283, filed on 30 Aug 1989, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Robinson, Douglas W.; Assistant Examiner: Harle, Jennifer
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN 14 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 8823
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods of treatment of subjects with systemic toxicity by administering an R'-Glu-Trp-R" pharmaceutical preparation.

L3 ANSWER 42 OF 59 USPATFULL
AN 1998:68822 USPATFULL
TI Cysteine-pegylated proteins
IN Braxton, Scott M., San Mateo, CA, United States
PA Incyte Pharmaceuticals, Inc., Palo Alto, CA, United States (U.S. corporation)
PI US 5766897 19980616
AI US 1995-427100 19950421 (8)
RLI Continuation-in-part of Ser. No. US 1993-144758, filed on 29 Oct 1993, now abandoned which is a continuation-in-part of Ser. No. US 1992-924294, filed on 3 Aug 1992, now patented, Pat. No. US 5457090 which is a continuation of Ser. No. US 1990-542484, filed on 21 Jun 1990, now patented, Pat. No. US 5187089, issued on 16 Feb 1993
DT Utility
FS Granted
EXNAM Primary Examiner: Hendricks, Keith D.; Assistant Examiner: Hobbs, Lisa J.
LREP Fish & Richardson P.C.
CLMN Number of Claims: 10
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 2765
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Methods and compositions are provided for the production of PEGylated proteins having polyethylene glycol covalently bound to a cysteine residue present in either the naturally-occurring protein or introduced by site-specific mutation. Where the cysteine residue is introduced by mutation, the site for mutation is selected on the basis of the presence of an N-linked glycosylation site or the position of the residue which

is normally solvent-accessible in the naturally-occurring protein. The modified proteins produced by the method of the invention are referred to as cysteine-PEGylated proteins. Proteins PEGylated according to the invention have increased half-lives following administration to a subject and decreased immunogenicity and antigenicity, while retaining substantially the same level of biological activity as that of the naturally-occurring, unmodified protein. Modification of proteins according to methods of the invention thus provide improved pharmaceutical compositions.

L3 ANSWER 43 OF 59 USPATFULL
AN 1998:68519 USPATFULL
TI Systemic gene treatment of connective tissue diseases with IRAP-1
IN Evans, Christopher H., Pittsburgh, PA, United States
Robbins, Paul D., Pittsburgh, PA, United States
PA University of Pittsburgh of the Commonwealth System of Higher Education, Pittsburgh, PA, United States (U.S. corporation)
PI US 5766585 19980616
AI US 1996-697180 19960820 (8)
RLI Continuation of Ser. No. US 1993-167642, filed on 14 Dec 1993, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Stanton, Brian R.
LREP Meyers, Diane R.Eckert Seamans Cherin & Mellott, LLC
CLMN Number of Claims: 3
ECL Exemplary Claim: 1
DRWN 2 Drawing Figure(s); 2 Drawing Page(s)
LN.CNT 1869
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to methods of therapeutic or prophylactic treatment of connective tissue diseases by systemic or local delivery of a nucleic acid sequence to a mammalian host. Expression of the nucleic acid sequence results in the systemic delivery of a biologically active protein or peptide which acts to antagonize inflammatory, hypertrophic and erosive phenomenon associated with connective tissue disease. Systemic delivery of such gene products results in sustained treatment of connective tissue diseases such as rheumatoid arthritis and systemic lupus erythematosus.

L3 ANSWER 44 OF 59 USPATFULL
AN 1998:57716 USPATFULL
TI Aptamers specific for biomolecules and methods of making
IN Griffin, Linda, Atherton, CA, United States
Albrecht, Glenn, Redwood City, CA, United States
Latham, John, Palo Alto, CA, United States
Leung, Lawrence, Hillsborough, CA, United States
Vermaas, Eric, Oakland, CA, United States
Toole, John J., Burlingame, CA, United States
PA Gilead Sciences, Inc., Foster City, CA, United States (U.S. corporation)
PI US 5756291 19980526
AI US 1995-484192 19950607 (8)
RLI Continuation of Ser. No. US 1992-934387, filed on 21 Aug 1992, now abandoned

DT Utility
FS Granted
EXNAM Primary Examiner: Zitomer, Stephanie W.
LREP Bosse, Mark L.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 6 Drawing Page(s)
LN.CNT 8242
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method for identifying oligomer sequences, optionally comprising modified base, which specifically bind target molecules such as serum proteins, kinins, eicosanoids and extracellular proteins is described. The method is used to generate aptamers that bind to serum Factor X, PDGF, FGF, ICAM, VCAM, E-selectin, thrombin, bradykinin, PGF2 and cell surface molecules. The technique involves complexation of the target molecule with a mixture of oligonucleotides containing random sequences and sequences which serve as primer for PCR under conditions wherein a complex is formed with the specifically binding sequences, but not with the other members of the oligonucleotide mixture. The complex is then separated from uncomplexed oligonucleotides and the complexed members of the oligonucleotide mixture are recovered from the separated complex using the polymerase chain reaction. The recovered oligonucleotides may be sequenced, and successive rounds of selection using complexation, separation, amplification and recovery can be employed. The oligonucleotides can be used for therapeutic and diagnostic purposes and for generating secondary aptamers.

L3 ANSWER 45 OF 59 USPATFULL
AN 1998:48215 USPATFULL
TI Method of detecting neutophil inhibitory factor mimics
IN Moyle, Matthew, Escondido, CA, United States
Foster, David L., Brighton, MA, United States
Vlasuk, George P., Carlsbad, CA, United States
PA Corvas International, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5747296 19980505
AI US 1993-173510 19931223 (8)
RLI Continuation-in-part of Ser. No. US 1993-151064, filed on 10 Nov 1993 which is a continuation-in-part of Ser. No. US 1993-60433, filed on 11 May 1993 which is a continuation-in-part of Ser. No. US 1992-996972, filed on 24 Dec 1992 which is a continuation-in-part of Ser. No. US 1992-881721, filed on 11 May 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Bashan, Daryl A.
LREP Lyon & Lyon LLP
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 65 Drawing Figure(s); 56 Drawing Page(s)
LN.CNT 5069
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions enriched for Neutrophil Inhibitory Factor which inhibit neutrophil activity including adhesion to vascular endothelial cells are provided. Also provided are recombinant Neutrophil Inhibitory Factors

which also which inhibit neutrophil activity. Such compositions may comprise a glycoprotein isolated from nematodes. These compositions and recombinant Neutrophil Inhibitory Factors are useful in the therapy of conditions which involve abnormal or undesired inflammatory responses.

L3 ANSWER 46 OF 59 USPATFULL
AN 1998:28061 USPATFULL
TI Methods for normalizing numbers of lymphocytes
IN Morozov, Vyacheslav G., St. Petersburg, Russian Federation
Khavinson, Vladimir Kh., St. Petersburg, Russian Federation
PA Cytoven J.V., Kirkland, WA, United States (U.S. corporation)
PI US 5728680 19980317
AI US 1995-452411 19950526 (8)
RLI Continuation-in-part of Ser. No. US 1994-337341, filed on 10 Nov 1994, now patented, Pat. No. US 5538951 And a continuation-in-part of Ser. No. US 1994-278463, filed on 21 Jul 1994, now abandoned which is a continuation-in-part of Ser. No. US 1994-257495, filed on 7 Jun 1994, now abandoned which is a continuation of Ser. No. US 1991-783518, filed on 28 Oct 1991, now abandoned which is a continuation-in-part of Ser. No. US 1991-678129, filed on 1 Apr 1991, now abandoned which is a continuation-in-part of Ser. No. US 1989-415283, filed on 30 Aug 1989, now abandoned
PRAI SU 1987-4352833 19871230
DT Utility
FS Granted
EXNAM Primary Examiner: Feisee, Lila; Assistant Examiner: Ungar, Susan
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN 16 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 8309
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides methods for normalizing the numbers of lymphocytes in animals by administering the dipeptide L-Glu-L-Trp.

L3 ANSWER 47 OF 59 USPATFULL
AN 97:91537 USPATFULL
TI Tri-substituted phenyl derivatives and processes for their preparation
IN Boyd, Ewan Campbell, Slough, United Kingdom
Eaton, Michael Anthony William, Watlington, United Kingdom
Warrellow, Graham John, Northwood, United Kingdom
PA Celltech Therapeutics Limited, Slough, United Kingdom (non-U.S. corporation)
PI US 5674880 19971007
AI US 1995-465871 19950606 (8)
RLI Division of Ser. No. US 1995-387551, filed on 13 Feb 1995, now patented, Pat. No. US 5491147 which is a continuation of Ser. No. US 1993-141873, filed on 22 Oct 1993, now abandoned
PRAI GB 1992-22253 19921023
DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra N.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris LLP
CLMN Number of Claims: 24
ECL Exemplary Claim: 1

DRWN No Drawings
LN.CNT 1499
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (1) ##STR1## are described wherein Y represents a halogen atom or a group --OR.sup.1, where R.sup.1 is an optionally substituted alkyl group; R.sup.2 represents an optionally substituted cycloalkyl or cycloalkenyl group; R.sup.3 is a monocyclic or bicyclic aryl group optionally containing one or more heteroatoms selected from oxygen or sulphur atoms or a group --N(R.sup.4)-- where R.sup.4 is a hydrogen atom or an alkyl group; X is --O--, --S--, or --N(R.sup.4)--, where R.sup.5 is a hydrogen or an alkyl group; with the proviso that when X is --O-- then R.sup.3 is not a 3-cyanamino-6-pyridazinyl or a 3-chloro-6-pyridazinyl group; and the salts, solvates, hydrates and N-oxides thereof.

The compounds are selective and potent inhibitors of phosphodiesterase IV and are useful for the prophylaxis and treatment of inflammatory diseases and the alleviation of conditions associated with central nervous malfunction.

L3 ANSWER 48 OF 59 USPATFULL
AN 97:33772 USPATFULL
TI Tri-substituted (aryl or heteroaryl) derivatives and pharmaceutical compositions containing the same
IN Warrellow, Graham J., Northwood, United Kingdom
Boyd, Ewan C., Slough, United Kingdom
Alexander, Rikki P., High Wycombe, United Kingdom
Head, John C., Windor, United Kingdom
PA Celltech Therapeutics Limited, Slough, United Kingdom (non-U.S. corporation)
PI US 5622977 19970422
AI US 1995-474214 19950607 (8)
RLI Continuation-in-part of Ser. No. US 1993-171822, filed on 22 Dec 1993, now abandoned
PRAI GB 1992-26831 19921223
GB 1993-15966 19930802
DT Utility
FS Granted
EXNAM Primary Examiner: Chang, Ceila
LREP Woodcock Washburn Kurtz MacKieiwcz & Norris
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 3661
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of the general formula (1) ##STR1## are described wherein Y is halogen or --OR.sup.1, where R.sup.1 is a substituted or unsubstituted alkyl; X is --O--, --S-- or --N(R.sup.8)--, where R.sup.8 is hydrogen or alkyl; R.sup.2 is substituted or unsubstituted alkyl, alkenyl, cycloalkyl or cycloalkenyl; R.sup.3 is hydrogen, halogen or --OR.sup.9, where R.sup.9 is hydrogen or substituted or unsubstituted alkyl, alkenyl, alkoxyalkyl, or alkanoyl, or formyl, carboxamido or thiocarboxamido; R.sup.4 and R.sup.5, which may be the same or different, are each --(CH.sub.2).sub.n Ar, where Ar is a monocyclic or

bicyclic aryl group or monocyclic or bicyclic heteroaryl and n is integer of 0 to 3; R.sup.6 is hydrogen or substituted or unsubstituted alkyl; R.sup.7 is hydrogen or substituted or unsubstituted alkyl; and the salts, solvates, hydrates and N-oxides thereof. Compounds according to the invention are potent, selective and orally active PDE IV inhibitors and are useful in the prophylaxis and treatment of asthma and other diseases.

L3 ANSWER 49 OF 59 USPATFULL
AN 96:80396 USPATFULL
TI Antibodies that specifically bind to and inhibit human synovial phospholipase A.sub.2 type A
IN Johnson, Lorin K., Pleasanton, CA, United States
Seilhamer, Jeffrey J., Milpitas, CA, United States
Pruzanski, Waldemar, Willowdale, Canada
Vadas, Peter, Toronto, Canada
PA Eli Lilly & Company, Indianapolis, IN, United States (U.S. corporation)
PI US 5552530 19960903
AI US 1994-283793 19940801 (8)
RLI Division of Ser. No. US 1993-58988, filed on 5 May 1993, now abandoned which is a continuation of Ser. No. US 1991-750230, filed on 19 Aug 1991, now abandoned which is a continuation of Ser. No. US 1990-579263, filed on 4 Sep 1990, now abandoned which is a continuation of Ser. No. US 1988-231865, filed on 16 Aug 1988, now abandoned which is a continuation-in-part of Ser. No. US 1988-215726, filed on 6 Jul 1988, now patented, Pat. No. US 5019508 which is a continuation-in-part of Ser. No. US 1987-89883, filed on 27 Aug 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Hutzell, Paula K.
LREP Morrison & Foerster
CLMN Number of Claims: 8
ECL Exemplary Claim: 1
DRWN 18 Drawing Figure(s); 18 Drawing Page(s)
LN.CNT 1481
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Antibodies that specifically bind to and inhibit the enzymatic activity of synovial phospholipase A.sub.2 Type A are described. The antibodies may be used in assays for detection of synovial phospholipase A.sub.2 in biological samples.

L3 ANSWER 50 OF 59 USPATFULL
AN 96:12868 USPATFULL
TI Tri-substituted phenyl derivatives and their use in pharmaceutical compositions and methods of treatment
IN Boyd, Ewan C., Slough, United Kingdom
Eaton, Michael A. W., Watlington, United Kingdom
Warrellow, Graham J., Northwood, United Kingdom
PA Celltech, Limited, Slough, United Kingdom (non-U.S. corporation)
PI US 5491147 19960213
AI US 1995-387551 19950213 (8)
RLI Continuation of Ser. No. US 1993-141873, filed on 22 Oct 1993, now abandoned
PRAI GB 1992-22253 19921023

DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra N.
LREP Woodcock Washburn Kurtz Mackiewicz & Norris
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1469
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compounds of formula (1) ##STR1## are described wherein Y represents a halogen atom or a group --OR.sup.1, where R.sup.1 is an optionally substituted alkyl group; R.sup.2 represents an optionally substituted cycloalkyl or cycloalkenyl group; R.sup.3 is a monocyclic or bicyclic aryl group optionally containing one or more heteroatoms selected from oxygen or sulphur atoms or a group --N(R.sup.4)-- where R.sup.4 is a hydrogen atom or an alkyl group; X is --O--, --S--, or --N(R.sup.5)--, where R.sup.5 is a hydrogen or an alkyl group; with the proviso that when X is --O-- then R.sup.3 is not a 3-cyanamino-6-pyridazinyl or a 3-chloro-6-pyridazinyl group; and the salts, solvates, hydrates and N-oxides thereof.

The compounds are selective and potent inhibitors of phosphodiesterase IV and are useful for the prophylaxis and treatment of inflammatory diseases and the alleviation of conditions associated with central nervous malfunction.

L3 ANSWER 51 OF 59 USPATFULL
AN 95:103251 USPATFULL
TI Avirulent microbes and uses therefor
IN Curtiss, III, Roy, St. Louis, MO, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 5468485 19951121
AI US 1993-20259 19930218 (8)
DCD 20110315
RLI Continuation of Ser. No. US 1989-332285, filed on 31 Mar 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-200934, filed on 1 Jun 1988, now abandoned which is a continuation-in-part of Ser. No. US 1987-58360, filed on 4 Jun 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Sidberry, Hazel F.
LREP Rogers, Howell & Haferkamp
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 2597
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a ***vaccine*** for the immunization of a vertebrate or invertebrate comprising an avirulent derivative of S. choleraesuis. The derivatives being substantially incapable of producing functional adenylate cyclase and/or cyclic AMP receptor protein. The invention also provides a ***vaccine*** for the immunization of a vertebrate and invertebrate comprising a virulent derivative of a pathogenic microbe said derivative being substantially incapable of

producing functional adenylate cyclase and/or cyclic AMP receptor protein while being capable of expressing a recombinant gene derived from a pathogen of said vertebrate to produce an antigen capable of inducing an immune response in said vertebrate against said pathogen.

L3 ANSWER 52 OF 59 USPATFULL
AN 95:13604 USPATFULL
TI Avirulent microbes and uses therefor
IN Gurtiss, III, Roy, St. Louis, MO, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 5389368 19950214
AI US 1992-965607 19921022 (7)
DCD 20110315
RLI Continuation of Ser. No. US 1988-200934, filed on 1 Jun 1988, now abandoned which is a continuation-in-part of Ser. No. US 1987-58360, filed on 4 Jun 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Low, Christopher S. F.
LREP Rogers, Howell & Haferkamp
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 2106
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a ***vaccine*** for the immunization of a vertebrate or invertebrate comprising an avirulent derivative of a pathogenic microbe said derivative being substantially incapable of producing functional adenylate cyclase and cyclic AMP receptor protein. The invention also provides a ***vaccine*** for the immunization of a vertebrate and invertebrate comprising a virulent derivative of a pathogenic microbe said derivative being substantially incapable of producing functional adenylate cyclase and cyclic AMP receptor protein while being capable of expressing a recombinant gene derived from a pathogen of said vertebrate to produce and antigen capable of inducing an immune response in said vertebrate against said pathogen.

L3 ANSWER 53 OF 59 CAPLUS COPYRIGHT 2001 ACS
AN 1993:219839 CAPLUS
DN 118:219839
TI ***Vaccines*** protective against gram-negative bacteremia, ***endotoxic*** ***shock*** , and related diagnostic assays
IN Apicella, Michael A.; Ward, Ronald E.; McNamara-Ward, Mary; Su, Shidong
PA Research Foundation of State University of New York, USA; Health Research Inc.
SO Can. Pat. Appl., 55 pp.
CODEN: CPXXEB
DT Patent
LA English
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
PI CA 2071069	AA	19930127	CA 1992-2071069	19920611
PRAI US 1991-736695		19910726		

AB Monoclonal anti-idiotype antibodies which mimic a common antigenic determinant on the lipid A portion of the lipopolysaccharide (LPS) of gram-neg. bacteria are developed and used as immunogens in ***vaccines*** designed to protect against gram-neg. bacteremia and septic shock. Thus, mice were immunized with heat-killed Re595 Salmonella minnesota and received ***Re*** 595 LPS. Primed spleen cells were fused at a 1:1 ratio with P3-X63-Ag8.653 cells and resulting clones were tested for binding to LPS and expanded. The anti-LPS response of mice, rabbits, and chickens was studied for idiotopic specificity.

L3 ANSWER 54 OF 59 USPATFULL
AN 93:26874 USPATFULL
TI Lipopolysaccharides of reduced toxicity and the production thereof
IN Munford, Robert S., Dallas, TX, United States
Hall, Catherine L., Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 5200184 19930406
AI US 1991-728763 19910708 (7)
RLI Continuation of Ser. No. US 1990-515657, filed on 24 Apr 1990, now abandoned which is a continuation of Ser. No. US 1987-53044, filed on 22 May 1987, now abandoned which is a continuation-in-part of Ser. No. US 1986-868428, filed on 28 May 1986, now patented, Pat. No. US 4929604
DT Utility
FS Granted
EXNAM Primary Examiner: Patterson, Jr., Charles L.
LREP Arnold, White & Durkee
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 781
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An acyloxyacyl hydrolase from the human promyelocyte cell line HL-60 has been found to specifically hydrolyze fatty acids from their ester linkages to hydroxy groups of 3-hydroxyfatty acids, the latter being bound in turn to LPS glycosaminyl residues. The hydrolyzed fatty acids may include dodecanoic acid, tetradecanoic acid and hexadecanoic acid. This enzyme showed a molecular weight by gel exclusion chromatography between about 50,000 Daltons and about 70,000 Daltons.

Altered bacterial LPS substantially without fatty acids bound in ester linkage to hydroxy groups of 3-hydroxyfatty acids covalently linked to a glucosaminyl moiety of LPS lipid A are produced. Since the structure of the lipid A moiety is highly conserved, ac

The U.S. Government may have rights in the present invention because the development was partially supported by NIH grant R01 AI18188 from the Department of Health and Human Services.

L3 ANSWER 55 OF 59 USPATFULL
AN 92:100995 USPATFULL
TI Diequatorially bound .beta.-1, 4 polyuronates and use of same for cytokine stimulation
IN Otterlei, Marit, Trondheim, Norway

Espevik, Terje, Trondheim, Norway
Skjak-Brock, Gudmund, Trondheim, Norway
Smidsrod, Olav, Trondheim, Norway
PA Nobipols Forskningsstiftelse, Trondheim, Norway (non-U.S. corporation)
Protan Biopolymer A/S, Drammen, Norway (non-U.S. corporation)
PI US 5169840 19921208
AI US 1991-676103 19910327 (7)
DT Utility
FS Granted
EXNAM Primary Examiner: Griffin, Ronald W.
LREP Blakely, Sokoloff, Taylor & Zafman
CLMN Number of Claims: 16
ECL Exemplary Claim: 1,15
DRWN 7 Drawing Figure(s); 5 Drawing Page(s)
LN.CNT 689
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to a material and method for the stimulation of the production of cytokines. Several polysaccharides, including polymers of different size of .sym.1-4 linked D-mannuronic acid (poly-M and M-blocks), chitosan and cellulose oxidized in C-6 position C60XY) induce human monocytes to produce the cytokines. Preferably, the molecular weights of poly-M and chitosan are above 50,000 and 20,000 respectively. Pretreatment of the monocytes with IFN-.gamma. increases the cytokine production from monocytes stimulated with all polysaccharides tested. The subject polysaccharides worked in vivo and in vitro.

The present invention has therapeutic utility as ***vaccine*** adjuvants and components. Therapeutic compositions comprising biologically active quantities of the compositions of the present invention may be employed to potentiate antibody production in response to ***vaccine*** antigens. Anti-tumor, anti-bacteriological, anti-fungal and anti-viral effects may be expected.

L3 ANSWER 56 OF 59 USPATFULL
AN 92:89050 USPATFULL
TI Method of stimulating the immune systems of animals and compositions useful therefor
IN Takayama, Kuni K., Madison, WI, United States
Qureshi, Nilofer, Madison, WI, United States
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 5158939 19921027
AI US 1990-522446 19900511 (7)
RLI Continuation-in-part of Ser. No. US 1989-383832, filed on 21 Jul 1989, now abandoned And a continuation-in-part of Ser. No. US 1990-467449, filed on 19 Jan 1990, now patented, Pat. No. US 5041427
DT Utility
FS Granted
EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: White, Everett
LREP Quarles & Brady
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings

LN.CNT 1426
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is disclosed for stimulating the immune systems of animals with non-toxic lipid A derivatives. The derivatives include the lipopolysaccharide (LPS) and diphosphoryl lipid A (DPLA) for Rhodopsuedomonas.

L3 ANSWER 57 OF 59 USPATFULL
AN 91:42649 USPATFULL
TI Synovial phospholipases
IN Johnson, Lorin K., Pleasanton, CA, United States
Seilhamer, Jeffrey J., Milpitas, CA, United States
Pruzanski, Waldemar, Ontario, Canada
Vadas, Peter, Ontario, Canada
PA Biotechnology Research Partners, Ltd., Ontario, CA, United States (U.S. corporation)
The University of Toronto Innovations Foundation, Ontario, Canada (non-U.S. corporation)
PI US 5019508 19910528
AI US 1988-215726 19880706 (7)
RLI Continuation-in-part of Ser. No. US 1987-89883, filed on 27 Aug 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartz, Richard A.; Assistant Examiner: Lebovitz, Richard
LREP Irell & Manella
CLMN Number of Claims: 25
ECL Exemplary Claim: 12
DRWN 12 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 1397
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Mammalian synovial phospholipase A.sub.2 (sPLA.sub.2) enzymes are provided, as well as DNA constructs encoding these enzymes, methods of producing the enzymes recombinantly, and antibodies thereto. Therapeutic methods employing anti-synovial phospholipase antibodies are also provided, in addition to diagnositc methods and other applications of sPLA.sub.2.

L3 ANSWER 58 OF 59 USPATFULL
AN 90:42500 USPATFULL
TI Lipopolysaccharides of reduced toxicity and the production thereof
IN Munford, Robert S., Dallas, TX, United States
Hall, Catherine L., Dallas, TX, United States
PA Board of Regents, The University of Texas System, Austin, TX, United States (U.S. corporation)
PI US 4929604 19900529
AI US 1986-868428 19860528 (6)
DT Utility
FS Granted
EXNAM Primary Examiner: Wiseman, Thomas G.; Assistant Examiner: Patterson, Jr., Charles L.
LREP Arnold, White & Durkee
CLMN Number of Claims: 14

ECL Exemplary Claim: 1
DRWN 5 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 709
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB An acyloxyacyl hydrolase from the human promyelocyte cell line HL-60 has been found to specifically hydrolyze fatty acids form their ester linkages to hydroxy groups of 3-hydroxyfatty acids, the latter being bound in turn to LPS glycosaminyl residues. The hydrolyzed fatty acids may include dodecanoic acid, tetradecanoic acid and hexadecanoic acid. This enzyme showed a molecular weight between about 50,000 daltons and about 70,000 daltons.

Altered bacterial LPS substantially without fatty acids bound in ester linkage to hydroxy groups of 3-hydroxyfatty acids covalently linked to a glucosaminyl moiety of LPS lipid A are produced. Since the structure of the lipid A moiety is highly conserved, acyloxyacyl hydrolase may act on LPS of many different pathogenic bacteria (for example Salmonella, Escherichia, Hemophilus, and Neisseria).

Such altered bacterial LPS, having toxicity reduced more than immunostimulatory activity, may be therapeutically useful: (1) as ***vaccines*** to prevent Gram-negative bacterial diseases by inducing antibodies to LPS 0-polysaccharide or R-core antigens, (2) as antidotes to treat or prevent gram-negative bacterial sepsis ("septic shock"), or (3) as adjuvants to enhance formation of antibodies to other antigens. The acyloxyacyl hydrolase itself may be therapeutically useful to detoxify endogenous LPS in patients with gram-negative bacterial diseases or to remove toxic LPS from therapeutic injectants.

L3 ANSWER 59 OF 59 EMBASE COPYRIGHT 2001 ELSEVIER SCI. B.V.DUPLICATE 1
AN 80042341 EMBASE
DN 1980042341
TI Enhancement of ***endotoxic*** ***shock*** by N-acetylmuramyl-L-alanyl-(L-seryl)-D-isoglutamine (muramyl dipeptide).
AU Ribi E.E.; Cantrell J.L.; Von Eschen K.B.; Schwartzman S.M.
CS Lab. Microbial Structure Funct., Nat. Inst. Allergy Infect. Dis., NIH, USDHEW, Rocky Mountain Lab., Hamilton, Mont. 59840, United States
SO Cancer Research, (1979) 39/11 (4756-4759).
CODEN: CNREA8
CY United States
DT Journal
FS 037 Drug Literature Index
016 Cancer
030 Pharmacology
LA English
AB We described elsewhere that the synergistic antitumor activity of endotoxic extracts from ***Re*** mutants of gram-negative bacteria and trehalose mycolate against guinea pig syngeneic line 10 tumor was abrogated after peptidic substances accompanying these extracts had been removed. This activity could be restored by combining peptide-free endotoxin either with cell wall skeleton from Bacillus Calmette-Guerin, a polymeric mycolic acid-arabinogalactan-mucopeptide complex, or with a combination of two components, trehalose dimycolate and N-acetylmuramyl-L-alanyl-(L-seryl)-D-isoglutamine (MDP). We report here

that when a combination of endotoxin (150 .mu.g) and a mixture of MDP (150.mu.g) and trehalose dimycolate (150.mu.g) was inoculated into established dermal tumors, a significant number of the animals died, presumably of ***endotoxic*** ***shock*** . All surviving animals suffered severe but temporary lethargy When administered alone intradermally in the dose levels tested, none of the components caused severe lethargy or lethality. The lethal effects of 150 .mu.g of MDP also occurred in combination with relatively weak endotoxic products, such as Pseudomonas ***vaccine*** (Pseudogen), and these effects did not depend upon the presence of malignant tissue. Guinea pigs inoculated I.V. were even more susceptible inasmuch as the addition of as little as 6 .mu.g of MDP to 150 .mu.g of Pseudogen, itself not lethal, caused the death of 80% of the animals.

=> d bib ab l4 1-
YOU HAVE REQUESTED DATA FROM 26 ANSWERS - CONTINUE? Y/(N):y

L4 ANSWER 1 OF 26 USPATFULL
AN 2001:163320 USPATFULL
TI Anti-interleukin-1 receptor antagonist antibodies and uses thereof
IN Ford, John, San Mateo, CA, United States
Pace, Ann, Scotts Valley, CA, United States
PA Hyseq, Inc., Sunnyvale, CA, United States (U.S. corporation)
PI US 6294655 B1 20010925
AI US 1999-417455 19991013 (9)
RLI Continuation-in-part of Ser. No. US 1999-348942, filed on 7 Jul 1999 Continuation of Ser. No. US 1999-287210, filed on 5 Apr 1999, now abandoned Continuation-in-part of Ser. No. US 1999-251370, filed on 17 Feb 1999, now abandoned Continuation-in-part of Ser. No. US 1998-127698, filed on 31 Jul 1998, now abandoned Continuation-in-part of Ser. No. US 1999-229591, filed on 13 Jan 1999, now abandoned Continuation of Ser. No. US 1998-99818, filed on 19 Jun 1998, now abandoned , said Ser. No. US 127698 Continuation-in-part of Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned , said Ser. No. US 99818 Continuation-in-part of Ser. No. US 1998-82364, filed on 20 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-79909, filed on 15 May 1998, now abandoned Continuation-in-part of Ser. No. US 1998-55010, filed on 3 Apr 1998, now abandoned
DT Utility
FS GRANTED
EXNAM Primary Examiner: Spector, Lorraine
LREP Marshall, O'Toole Gerstein, Murray & Borun
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 15 Drawing Figure(s); 14 Drawing Page(s)
LN.CNT 4656
AB The present invention provides novel nucleic acids, the novel polypeptide sequences encoded by these nucleic acids and uses thereof. These novel polynucleotide and polypeptide sequences were determined to be a novel Interleukin-1 Receptor Antagonist. Also provided are antibodies which bind the antagonist, methods of detecting the antagonist, and kits containing the antibodies.

L4 ANSWER 2 OF 26 USPATFULL
AN 2001:152960 USPATFULL
TI Substituted 4-biarylbutyric and 5-biarylpentanoic acid derivatives as matrix metalloprotease inhibitors
IN Kluender, Harold Clinton Eugene, Trumbull, CT, United States
Brittelli, David Ross, Branford, CT, United States
Schoen, William Riley, Madison, CT, United States
Ha, Sookhee Nicole, Woodbridge, CT, United States
PA Bayer Corporation, Pittsburgh, PA, United States (U.S. corporation)
PI US 6288063 B1 20010911
AI US 1998-85909 19980527 (9)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Shah, Mukund J.; Assistant Examiner: Rao, Deepak R.
CLMN Number of Claims: 13
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 2207
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Inhibitors for matrix metalloproteases, pharmaceutical compositions containing them, and a process for using them to treat a variety of physiological conditions. The compounds of the invention have the generalized formula

(T).sub.x A--B--D--E--G

wherein A is an aryl or heteroaryl rings; B is an aryl or heteroaryl ring or a bond; each T is a substituent group; x is 0, 1, or 2; the group D represents ##STR1##

the group E represents a two or three carbon chain bearing one to three substituent groups which are independent or are involved in ring formation, possible structures being shown in the text and claims; and the group G represents ##STR2##

and with the proviso that when G is ##STR3##

each of the substituents on E is an independent substituent; and include pharmaceutically acceptable salts thereof.

L4 ANSWER 3 OF 26 USPATFULL
AN 2001:136190 USPATFULL
TI Hemoglobin receptors from neisseriae
IN Stojiljkovic, Igor, Portland, OR, United States
So, Magdalene, Portland, OR, United States
Hwa, Vivian, Portland, OR, United States
Heffron, Fred, West Linn, OR, United States
Nassif, Xavier, Paris, France
PA Oregon Health Sciences University, Portland, OR, United States (U.S. corporation)
PI US 6277382 B1 20010821
WO 9612020 19960425
AI US 1997-817707 19970819 (8)
WO 1995-US13623 19951017

19970819 PCT 371 date
19970819 PCT 102(e) date
DT Utility
FS GRANTED
EXNAM Primary Examiner: Graser, Jennifer
LREP McDonnell Boehnen Hulbert & Berghoff
CLMN Number of Claims: 5
ECL Exemplary Claim: 1
DRWN 11 Drawing Figure(s); 47 Drawing Page(s)
LN.CNT 1750
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel bacterial hemoglobin receptor proteins and genes that encode such proteins. The invention is directed toward the isolation, characterization, diagnostic and therapeutic use of bacterial hemoglobin receptor proteins, nucleic acids encoding such proteins, recombinant expression constructs comprising such nucleic acids and cells transformed therewith, and antibodies and epitopes of such hemoglobin receptor proteins. The invention relates particularly to hemoglobin receptor proteins and genes encoding such proteins from Neisseria species, especially N. meningitidis and serotypes thereof, and N. gonorrhoeae. Methods for the diagnostic and therapeutic use of the proteins, epitopes, antibodies and nucleic acids of the invention are also provided, including the use of proteins, epitopes, antibodies and nucleic acids of the invention for the production of ***vaccines*** effective in providing immunization of human against infection by pathogenic bacteria of Neisseria species.

L4 ANSWER 4 OF 26 USPATFULL
AN 2001:117039 USPATFULL
TI Pyrrolidine modulators of chemokine receptor activity
IN Caldwell, Charles, Scotch Plains, NJ, United States
Chapman, Kevin T., Scotch Plains, NJ, United States
Hale, Jeffrey, Westfield, NJ, United States
Kim, Dooseop, Westfield, NJ, United States
Lynch, Christopher, Scotch Plains, NJ, United States
MacCoss, Malcolm, Freehold, NJ, United States
Mills, Sander G., Scotch Plains, NJ, United States
Rosauer, Keith, Matawan, NJ, United States
Willoughby, Christopher, Edison, NJ, United States
Berk, Scott, Maplewood, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6265434 B1 20010724
AI US 2000-543024 20000404 (9)
PRAI US 1999-128035 19990406 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Raymond, Richard L.; Assistant Examiner: Patel, Sudhaker B.
LREP Walton, Kenneth R., Winokur, Melvin
CLMN Number of Claims: 36
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 8546
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB The present invention is directed to pyrrolidine compounds of the formula 1: ##STR1##

(wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6 and n are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3.

L4 ANSWER 5 OF 26 USPATFULL
AN 2001:108030 USPATFULL
TI Inhibitors of Interleukin-1.beta. converting enzyme
IN Batchelor, Mark James, Cumnor Hill, United Kingdom
Bebbington, David, Pewsey, United Kingdom
Bemis, Guy W., Arlington, MA, United States
Fridman, Wolf Herman, Paris, France
Gillespie, Roger John, Oaksey, United Kingdom
Golec, Julian M. C., Ashbury, United Kingdom
Gu, Yong, Brookline, MA, United States
Lauffer, David J., Stow, MA, United States
Livingston, David J., Newtonville, MA, United States
Matharu, Saroop Singh, Cricklade, United Kingdom
Mullican, Michael D., Needham, MA, United States
Murcko, Mark A., Holliston, MA, United States
Murdoch, Robert, Highworth, United Kingdom
Nyce, Philip, Milbury, MA, United States
Robidoux, Andrea L. C., Andover, MA, United States
Su, Michael, Newton, MA, United States
Wannamaker, M. Woods, Stow, MA, United States
Wilson, Keith P., Hopkinton, MA, United States
Zelle, Robert E., Stow, MA, United States
PA Vertex Pharmaceuticals, Incorporated, Cambridge, MA, United States (U.S. corporation)
PI US 6258948 B1 20010710
AI US 1999-400639 19990921 (9)
RLI Division of Ser. No. US 1996-761483, filed on 6 Dec 1996 Continuation-in-part of Ser. No. US 1996-712878, filed on 12 Sep 1996, now patented, Pat. No. US 5985863 Continuation-in-part of Ser. No. US 1996-598332, filed on 8 Feb 1996, now patented, Pat. No. US 5874424 Continuation-in-part of Ser. No. US 1995-575641, filed on 20 Dec 1995, now patented, Pat. No. US 6008217
PRAI US 1996-31495 19961126 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Kifle, Bruck
LREP Fish & Neave, Haley, Jr., Esq., James F., Joslyn, Kristin M.
CLMN Number of Claims: 46
ECL Exemplary Claim: 1
DRWN 21 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 13229
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel classes of compounds which are inhibitors of interleukin-IB converting enzyme. The ICE inhibitors of this invention are characterized by specific structural and physicochemical features. This invention also relates to pharmaceutical

compositions comprising these compounds. The compounds and pharmaceutical compositions of this invention are particularly well suited for inhibiting ICE activity and consequently, may be advantageously used as agents against IL-1-, apoptosis-, IGIF-, and IFN-.gamma.-mediated diseases, inflammatory diseases, autoimmune diseases, destructive bone disorders, proliferative disorders, infectious diseases, degenerative diseases, and necrotic diseases. This invention also relates to methods for inhibiting ICE activity, for treating interleukin-1-, apoptosis-, IGIF- and IFN-.gamma.-mediated diseases and decreasing IGIF and IFN-.gamma. production using the compounds and compositions of this invention. This invention also relates to methods for preparing N-acylamino compounds.

L4 ANSWER 6 OF 26 USPATFULL
AN 2001:93521 USPATFULL
TI Pyrrolidine modulators of chemokine receptor activity
IN Chapman, Kevin, Scotch Plains, NJ, United States
Hale, Jeffrey, Westfield, NJ, United States
Kim, Dooseop, Westfield, NJ, United States
Lynch, Christopher, Scotch Plains, NJ, United States
Shah, Shrenik, Metuchen, NJ, United States
Shankaran, Kothandaraman, Kendall Park, NJ, United States
Shen, Dong-Ming, Edison, NJ, United States
Willoughby, Christopher, Clark, NJ, United States
MacCoss, Malcolm, Freehold, NJ, United States
Mills, Sander G., Scotch Plains, NJ, United States
Loebach, Jennifer L., Westfield, NJ, United States
Guthikonda, Ravindra N., Edison, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6248755 B1 20010619
AI US 2000-542617 20000404 (9)
PRAI US 1999-128033 19990406 (60)
DT Utility
FS GRANTED
EXNAM Primary Examiner: Seaman, D. Margaret
LREP Walton, Kenneth R., Winokur, Melvin
CLMN Number of Claims: 39
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 9773
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to pyrrolidine compounds of the formula I: ##STR1##

(wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4, R.sup.5, R.sup.6, R.sup.14 and n are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-5 and/or CCR-3.

L4 ANSWER 7 OF 26 USPATFULL
AN 2001:40475 USPATFULL
TI Inhibitors of interleukin-1.beta. Converting enzyme inhibitors
IN Batchelor, Mark James, Cumnor Hill, United Kingdom
Bebbington, David, Pewsey, United Kingdom

Bemis, Guy W., Arlington, MA, United States
Fridman, Wolf Herman, Paris, France
Gillespie, Roger John, Malmesbury, United Kingdom
Golec, Julian M. C., Swindon, United Kingdom
Gu, Yong, Brookline, MA, United States
Lauffer, David J., Stow, MA, United States
Livingston, David J., Newtonville, MA, United States
Matharu, Saroop Singh, Cricklade, United Kingdom
Mullican, Michael D., Needham, MA, United States
Murcko, Mark A., Holliston, MA, United States
Murdoch, Robert, Highworth, United Kingdom
Nyce, Philip, Milbury, MA, United States
Robidoux, Andrea L. C., Andover, MA, United States
Su, Michael, Newton, MA, United States
Wannamaker, M. Woods, Stow, MA, United States
Wilson, Keith P., Hopkinton, MA, United States
Zelle, Robert E., Stow, MA, United States
PA Vertex Pharmaceuticals Incorporated, Cambridge, MA, United States (U.S. corporation)
PI US 6204261 B1 20010320
AI US 1996-761483 19961206 (8)
RLI Continuation-in-part of Ser. No. US 1996-712878, filed on 12 Sep 1996 Continuation-in-part of Ser. No. US 1996-598332, filed on 8 Feb 1996, now patented, Pat. No. US 5874424 Continuation-in-part of Ser. No. US 1995-575641, filed on 20 Dec 1995
PRAI US 1996-31495 19961126 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Gupta, Yogendra N.; Assistant Examiner: Kifle, Bruck
LREP Fish & Neave, Haley, Jr., James F., Dixon, Lisa A.
CLMN Number of Claims: 34
ECL Exemplary Claim: 1
DRWN 20 Drawing Figure(s); 11 Drawing Page(s)
LN.CNT 12975
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to pyradazino[1,2-a][1,2]diazepine-1-carboxamide compounds of formula: ##STR1##

which compounds are inhibitors of interleukin-1beta converting enzyme.

L4 ANSWER 8 OF 26 USPATFULL
AN 2001:14213 USPATFULL
TI Method for diagnosing and treating chronic pelvic pain syndrome
IN Alexander, Richard B., Ellicott City, MD, United States
Ponniah, Sathibalan, Ellicott City, MD, United States
PA University of Maryland, Baltimore, Baltimore, MD, United States (U.S. corporation)
PI US 6180355 B1 20010130
AI US 1999-306927 19990507 (9)
PRAI US 1998-84668 19980507 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Schwartzman, Robert A.; Assistant Examiner: Larson, Thomas G.

LREP Hultquist, Steven J., Barrett, William A.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 3501
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides a superior method of diagnosing Chronic Pelvic Pain Syndrome in men comprising measuring levels of cytokines in semen or components or fractions of semen. The invention also provides a method of treating a condition associated with elevated levels of a cytokine, such as TNF-.alpha., in semen or a component or fraction thereof, comprising administering a therapeutically effective amount of an ant-cytokine compound or composition, such as an anti-TNF-.alpha. compound or composition.

L4 ANSWER 9 OF 26 USPATFULL
AN 2000:174663 USPATFULL
TI Pyrrolidine and piperidine modulators of chemokine receptor activity
IN Budhu, Richard J., Monmouth Junction, NJ, United States
Holson, Edward, New York, NY, United States
Hale, Jeffrey J., Westfield, NJ, United States
Lynch, Christopher, Scotch Plains, NJ, United States
Maccoss, Malcolm, Freehold, NJ, United States
Berk, Scott C., Maplewood, NJ, United States
Mills, Sander G., Scotch Plains, NJ, United States
Willoughby, Christopher A., Clark, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 6166037 20001226
AI US 1998-141227 19980827 (9)
PRAI US 1997-57743 19970828 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Chang, Ceila
LREP Thies, J. Eric, Rose, David L.
CLMN Number of Claims: 25
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 4273
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to pyrrolidine and piperidine compounds of the formula I: ##STR1## (wherein R.sup.1, R.sup.2, R.sup.3, R.sup.4a, R.sup.4b, R.sup.4c, R.sup.4d, R.sup.4e, R.sup.4f, R.sup.4g, R.sup.4h, m, n, x and y are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4.

L4 ANSWER 10 OF 26 USPATFULL
AN 2000:160799 USPATFULL
TI Death domain containing receptors
IN Yu, Guo-Liang, Darnestown, MD, United States
Ni, Jian, Rockville, MD, United States
Gentz, Reiner L., Silver Spring, MD, United States
Dillon, Patrick J., Gaithersburg, MD, United States

PA Human Genome Sciences, Inc., Rockville, MD, United States (U.S. corporation)
PI US 6153402 20001128
AI US 1997-815469 19970311 (8)
PRAI US 1996-13285 19960312 (60)
US 1996-28711 19961017 (60)
US 1997-37341 19970206 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Ulm, John
LREP Sterne, Kessler, Goldstein & Fox, P.L.L.C.
CLMN Number of Claims: 61
ECL Exemplary Claim: 1
DRWN 6 Drawing Figure(s); 10 Drawing Page(s)
LN.CNT 3364
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel Death Domain Containing Receptor (DR3 and DR3-V1) proteins which are members of the tumor necrosis factor (TNF) receptor family. In particular, isolated nucleic acid molecules are provided encoding the human DR3 and DR3-V1 proteins. DR3 and DR3-V1 polypeptides are also provided, as are vectors, host cells and recombinant methods for producing the same. The invention further relates to screening methods for identifying agonists and antagonists of DR3 and DR3-V1 activity.

L4 ANSWER 11 OF 26 USPATFULL
AN 2000:125014 USPATFULL
TI Neutrophil stimulating peptides
IN Rathien, Deborah Ann, Thornleigh, Australia
Ferrante, Antonio, Mount Osmond, Australia
PA Peptide Technology Limited, Australia (non-U.S. corporation)
PI US 6121237 20000919
AI US 1996-714960 19960917 (8)
RLI Division of Ser. No. US 1993-107235, filed on 16 Aug 1993, now patented, Pat. No. US 5587457 which is a continuation-in-part of Ser. No. US 1992-930415, filed on 9 Nov 1992, now abandoned
PRAI AU 1990-19065 19900312
WO 1991-AU86 19910312
DT Utility
FS Granted
EXNAM Primary Examiner: Russel, Jeffrey E.
LREP Banner & Witcoff, Ltd.
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1126
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides peptides capable of stimulating neutrophils. In particular, the peptides prime neutrophils for a respiratory burst following treatment with N-formyl-L-methionyl-L-leucyl-L-phenylalanine. The peptides have an amino acid sequence substantially corresponding to amino acids 54 to 94 of FIG. 1 or a part thereof. These peptides may also be used in the treatment of a subject having depressed neutrophil function.

L4 ANSWER 12 OF 26 USPATFULL
AN 2000:124815 USPATFULL
TI Bacterial hemoglobin receptor genes
IN Stojiljkovic, Igor, 3223 SW. 11th Ave. #3, Portland, OR, United States 97201
So, Magdalene, 777 SW. 48th Dr., Portland, OR, United States 97221
Hwa, Vivian, 7011 SW. 4th Ave., Portland, OR, United States 97219
Heffron, Fred, 17887 Hillside Dr., West Linn, OR, United States 97068
Nassif, Xavier, 36 Rue Miollis, Paris, France
PI US 6121037 20000919
AI US 1995-537361 19951002 (8)
RLI Continuation-in-part of Ser. No. US 1994-326670, filed on 18 Oct 1994, now patented, Pat. No. US 5698438
DT Utility
FS Granted
EXNAM Primary Examiner: Hutzell, Paula K.; Assistant Examiner: Hayes, Robert C.
CLMN Number of Claims: 4
ECL Exemplary Claim: 1
DRWN 47 Drawing Figure(s); 47 Drawing Page(s)
LN.CNT 3180
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention relates to novel bacterial hemoglobin receptor proteins and genes that encode such proteins. The invention is directed toward the isolation, characterization, diagnostic and therapeutic use of bacterial hemoglobin receptor proteins, nucleic acid encoding such proteins, recombinant expression constructs comprising such nucleic acids and cells transformed therewith, and antibodies and epitopes of such hemoglobin receptor proteins. The invention relates particularly to hemoglobin receptor proteins and genes encoding such proteins from Neisseria species, especially N. meningitidis and serotypes thereof, and N. gonorrhoeae. Methods for the diagnostic and therapeutic use of the proteins, epitopes, antibodies and nucleic acids of the invention are also provided, including the use of the proteins, epitopes, antibodies and nucleic acids of the invention for the production of ***vaccines*** effective in providing immunization of a human against infection by pathogenic bacteria of Neisseria species.

L4 ANSWER 13 OF 26 USPATFULL
AN 1999:159997 USPATFULL
TI Compounds that bind bacterial pili
IN Shekhani, Mohammed Saleh, Madison, WI, United States
Firca, Joseph R., Vernon Hills, IL, United States
Anderson, Byron, Morton Grove, IL, United States
PA Ophidian Pharmaceuticals, Inc., Madison, WI, United States (U.S. corporation)
PI US 5998381 19991207
AI US 1996-760903 19961206 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Peselev, Elli
LREP Medlen & Carroll, LLP
CLMN Number of Claims: 24

ECL Exemplary Claim: 5
DRWN 23 Drawing Figure(s); 25 Drawing Page(s)
LN.CNT 6570
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Diagnostics and treatments for bacterial infection are disclosed. The treatments prevent bacteria from adhering to host cells by interfering with the binding of the bacteria to cell receptors. Compounds that inhibit bacterial adherence to cells are engineered to be readily modified for best efficacy with different modes of treatment. The compounds can be readily modified for use to identify bacteria according to their cell binding specificities.

L4 ANSWER 14 OF 26 USPATFULL
AN 1999:75756 USPATFULL
TI Modified hookworm neutrophil inhibitors
IN Moyle, Matthew, Escondido, CA, United States
Foster, David L., Brighton, MA, United States
PA Corvas International, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5919900 19990706
AI US 1995-450497 19950526 (8)
RLI Division of Ser. No. US 1993-173510, filed on 23 Dec 1993 which is a continuation-in-part of Ser. No. US 1993-151064, filed on 10 Nov 1993 which is a continuation-in-part of Ser. No. US 1993-60433, filed on 11 May 1993 which is a continuation-in-part of Ser. No. US 1992-996972, filed on 24 Dec 1992 which is a continuation-in-part of Ser. No. US 1992-881721, filed on 11 May 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Fitzgerald, David L.; Assistant Examiner: Lathrop, Brian
LREP Lyon & Lyon LLP
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN 69 Drawing Figure(s); 56 Drawing Page(s)
LN.CNT 5740
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions enriched for Neutrophil Inhibitory Factor which inhibit neutrophil activity including adhesion to vascular endothelial cells are provided. Also provided are recombinant Neutrophil Inhibitory Factors which also which inhibit neutrophil activity. Such compositions may comprise a glycoprotein isolated from nematodes. These compositions and recombinant Neutrophil Inhibitory Factors are useful in the therapy of conditions which involve abnormal or undesired inflammatory responses.

L4 ANSWER 15 OF 26 USPATFULL
AN 1999:75632 USPATFULL
TI Substituted aminoquinolines as modulators of chemokine receptor activity
IN Hagmann, William K., Westfield, NJ, United States
Springer, Martin S., Westfield, NJ, United States
PA Merck & Co., Inc., Rahway, NJ, United States (U.S. corporation)
PI US 5919776 19990706
AI US 1997-993494 19971218 (8)
DT Utility

FS Granted
EXNAM Primary Examiner: Mach, D. Margaret M.
LREP Thies, J. Eric, Rose, David L.
CLMN Number of Claims: 12
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1808
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention is directed to aminoquinolines of Formula I: ##STR1## (wherein R.sup.1, R.sup.2, R.sup.3, and R.sup.4 are defined herein) which are useful as modulators of chemokine receptor activity. In particular, these compounds are useful as modulators of the chemokine receptors CCR-1, CCR-2, CCR-2A, CCR-2B, CCR-3, CCR-4, CCR-5, CXCR-3, and/or CXCR-4.

L4 ANSWER 16 OF 26 USPATFULL
AN 1999:36923 USPATFULL
TI DNA encoding tumor necrosis related receptor, TR4
IN Emery, John, Wynnewood, PA, United States
Tan, KB, Philadelphia, PA, United States
Truneh, Alemseged, West Chester, PA, United States
Young, Peter R., Lawrenceville, NJ, United States
PA Smithkline Beecham Corporation, Philadelphia, PA, United States (U.S. corporation)
PI US 5885800 19990323
AI US 1997-794796 19970204 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Draper, Garnette D.
LREP Han, William T., King, William T.
CLMN Number of Claims: 16
ECL Exemplary Claim: 1
DRWN 3 Drawing Figure(s); 3 Drawing Page(s)
LN.CNT 1027
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB TR4 polypeptides and polynucleotides and methods for producing such polypeptides by recombinant techniques are disclosed. Also disclosed are methods for utilizing TR4 polypeptides and polynucleotides in the design of protocols for the treatment of chronic and acute inflammation, arthritis, septicemia, autoimmune diseases (eg inflammatory bowel disease, psoriasis), transplant rejection, graft vs. host disease, infection, stroke, ischemia, acute respiratory disease syndrome, restenosis, brain injury, AIDS, Bone diseases, cancer (eg lymphoproliferative disorders), atheroschlerosis, and Alzheimers disease among others, and diagnostic assays for such conditions.

L4 ANSWER 17 OF 26 USPATFULL
AN 1998:147232 USPATFULL
TI Protease and related nucleic acid compounds
IN Ni, Binhui, Carmel, IN, United States
Paul, Marc, Carmel, IN, United States
Wu, Xin, Carmel, IN, United States
PA Eli Lilly and Company, Indianapolis, IN, United States (U.S. corporation)

PI US 5840509 19981124
AI US 1997-890542 19970709 (8)
DT Utility
FS Granted
EXNAM Primary Examiner: Jacobson, Dian C.
LREP Gaylo, Paul J., Boone, David E.
CLMN Number of Claims: 2
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1761
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides for a novel ICE related protease and nucleic acids coding same. The present invention also provides a method to isolate an ICE related protease and related DNA compounds encoding this protease. The present invention further comprises a method using said protease to screen for inhibitors of apoptosis. Additionally, the invention further comprises a method of using said inhibitors of apoptosis in the treatment in human patients with the acquired disease states of brain ischemia, stroke, Alzheimer's disease, amyotrophic lateral sclerosis (ALS), head trauma, or other neurodegenerative disorders.

L4 ANSWER 18 OF 26 USPATFULL
AN 1998:91809 USPATFULL
TI Neutrophil inhibitors
IN Moyle, Matthew, Escondido, CA, United States
Foster, David L., Brighton, MA, United States
Vlasuk, George P., Carlsbad, CA, United States
PA Corvas International, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5789178 19980804
AI US 1995-458218 19950602 (8)
RLI Continuation of Ser. No. US 1993-151064, filed on 10 Nov 1993 which is a continuation-in-part of Ser. No. US 1993-60433, filed on 11 May 1993 which is a continuation-in-part of Ser. No. US 1992-996972, filed on 24 Dec 1992 which is a continuation-in-part of Ser. No. US 1992-881721, filed on 11 May 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Basham, Daryl A.
LREP Lyon & Lyon LLP
CLMN Number of Claims: 29
ECL Exemplary Claim: 1
DRWN 65 Drawing Figure(s); 56 Drawing Page(s)
LN.CNT 5374
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions enriched for Neutrophil Inhibitory Factor which inhibit neutrophil activity including adhesion to vascular endothelial cells are provided. Also provided are recombinant Neutrophil Inhibitory Factors which also which inhibit neutrophil activity. Such compositions may comprise a glycoprotein isolated from nematodes. These compositions and recombinant Neutrophil Inhibitory Factors are useful in the therapy of conditions which involve abnormal or undesired inflammatory responses.

L4 ANSWER 19 OF 26 USPATFULL
AN 1998:48215 USPATFULL
TI Method of detecting neutophil inhibitory factor mimics
IN Moyle, Matthew, Escondido, CA, United States
Foster, David L., Brighton, MA, United States
Vlasuk, George P., Carlsbad, CA, United States
PA Corvas International, Inc., San Diego, CA, United States (U.S. corporation)
PI US 5747296 19980505
AI US 1993-173510 19931223 (8)
RLI Continuation-in-part of Ser. No. US 1993-151064, filed on 10 Nov 1993 which is a continuation-in-part of Ser. No. US 1993-60433, filed on 11 May 1993 which is a continuation-in-part of Ser. No. US 1992-996972, filed on 24 Dec 1992 which is a continuation-in-part of Ser. No. US 1992-881721, filed on 11 May 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Walsh, Stephen; Assistant Examiner: Bashan, Daryl A.
LREP Lyon & Lyon LLP
CLMN Number of Claims: 21
ECL Exemplary Claim: 1
DRWN 65 Drawing Figure(s); 56 Drawing Page(s)
LN.CNT 5069
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions enriched for Neutrophil Inhibitory Factor which inhibit neutrophil activity including adhesion to vascular endothelial cells are provided. Also provided are recombinant Neutrophil Inhibitory Factors which also which inhibit neutrophil activity. Such compositions may comprise a glycoprotein isolated from nematodes. These compositions and recombinant Neutrophil Inhibitory Factors are useful in the therapy of conditions which involve abnormal or undesired inflammatory responses.

L4 ANSWER 20 OF 26 USPATFULL
AN 1998:7088 USPATFULL
TI Tri-aryl ethane derivatives as PDE IV inhibitors
IN Guay, Daniel, Ile Perrot, Canada
Girard, Yves, Ille Bizard, Canada
Ducharme, Yves, Montreal, Canada
Blouin, Marc, St. Lazare, Canada
Hamel, Pierre, Laval, Canada
Girard, Mario, Montreal, Canada
PA Merck Frosst Canada, Inc., Kirkland, Canada (non-U.S. corporation)
PI US 5710170 19980120
AI US 1996-763566 19961210 (8)
PRAI US 1996-8204 19961215 (60)
DT Utility
FS Granted
EXNAM Primary Examiner: Ivy, C. Warren; Assistant Examiner: Mach, P. Margaret M.
LREP Panzer, Curtis C., Rose, David L.
CLMN Number of Claims: 9
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1708

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The invention encompasses the novel compound of Formula I useful in the treatment of diseases, including asthma, by raising the level of cyclic adenosine-3',5'-monophosphate (cAMP) through the inhibition of phosphodiesterase IV (PDE IV). ##STR1## The invention also encompasses certain pharmaceutical compositions and methods for treatment of diseases by inhibition of PDE IV, resulting in an elevation of cAMP, comprising the use of compounds of Formula I.

L4 ANSWER 21 OF 26 USPATFULL
AN 96:118669 USPATFULL
TI Neutrophil stimulating peptides
IN Rathjen, Deborah A., Thornleigh, Australia
Ferrante, Antonio, Mount Osmond, Australia
PA Peptide Technology Limited, Australia (non-U.S. corporation)
PI US 5587457 19961224
AI US 1993-107235 19930816 (8)
RLI Continuation-in-part of Ser. No. US 1992-930415, filed on 9 Nov 1992, now abandoned
PRAI AU 1990-9065 19900312
DT Utility
FS Granted
EXNAM Primary Examiner: Weimar, Elizabeth C.; Assistant Examiner: Marshall, S. G.
LREP Banner & Allegretti, Ltd.
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 1027
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB The present invention provides peptides capable of stimulating neutrophils. In particular, the peptides prime neutrophils for a respiratory burst following treatment with N-formyl-L-methionyl-L-leucyl-Lphenylalanine. The peptides have an amino acid sequence substantially corresponding to amino acids 54 to 94 of FIG. 1 or a part thereof. These peptides may also be used in the treatment of a subject having depressed neutrophil function.

L4 ANSWER 22 OF 26 USPATFULL
AN 96:72966 USPATFULL
TI Conjugates for the prevention and treatment of sepsis
IN Carroll, Sean B., Cottage Grove, WI, United States
Firca, Joseph R., Vernon Hills, IL, United States
Pugh, Charles, Madison, WI, United States
Padhye, Nisha V., Madison, WI, United States
PA Ophidian Pharmaceuticals, Inc., Madison, WI, United States (U.S. corporation)
PI US 5545721 19960813
AI US 1993-169701 19931217 (8)
RLI Continuation-in-part of Ser. No. US 1992-995388, filed on 21 Dec 1992, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Chan, Christina Y.; Assistant Examiner: Eisenschenk,

Frank C.
LREP Medlen & Carroll
CLMN Number of Claims: 30
ECL Exemplary Claim: 1
DRWN 17 Drawing Figure(s); 16 Drawing Page(s)
LN.CNT 4769
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB Compositions and methods are described for preventing and treating sepsis in humans and other animals. Surgical patients, low birth weight infants, burn and trauma victims, as well as other individuals at risk can be treated prophylactically. Methods for treating acute infections with advantages over current therapeutic approaches are provided. Conjugates and methods of making conjugates for the prevention and treatment of sepsis are described.

L4 ANSWER 23 OF 26 USPATFULL
AN 95:103251 USPATFULL
TI Avirulent microbes and uses therefor
IN Curtiss, III, Roy, St. Louis, MO, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 5468485 19951121
AI US 1993-20259 19930218 (8)
DCD 20110315
RLI Continuation of Ser. No. US 1989-332285, filed on 31 Mar 1989, now abandoned which is a continuation-in-part of Ser. No. US 1988-200934, filed on 1 Jun 1988, now abandoned which is a continuation-in-part of Ser. No. US 1987-58360, filed on 4 Jun 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Sidberry, Hazel F.
LREP Rogers, Howell & Haferkamp
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 2597
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a ***vaccine*** for the immunization of a vertebrate or invertebrate comprising an avirulent derivative of S. choleraesuis. The derivatives being substantially incapable of producing functional adenylate cyclase and/or cyclic AMP receptor protein. The invention also provides a ***vaccine*** for the immunization of a vertebrate and invertebrate comprising a virulent derivative of a pathogenic microbe said derivative being substantially incapable of producing functional adenylate cyclase and/or cyclic AMP receptor protein while being capable of expressing a recombinant gene derived from a pathogen of said vertebrate to produce an antigen capable of inducing an immune response in said vertebrate against said pathogen.

L4 ANSWER 24 OF 26 USPATFULL
AN 95:13604 USPATFULL
TI Avirulent microbes and uses therefor
IN Gurtiss, III, Roy, St. Louis, MO, United States
PA Washington University, St. Louis, MO, United States (U.S. corporation)
PI US 5389368 19950214

AI US 1992-965607 19921022 (7)
DCD 20110315
RLI Continuation of Ser. No. US 1988-200934, filed on 1 Jun 1988, now abandoned which is a continuation-in-part of Ser. No. US 1987-58360, filed on 4 Jun 1987, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Low, Christopher S. F.
LREP Rogers, Howell & Haferkamp
CLMN Number of Claims: 11
ECL Exemplary Claim: 1
DRWN 8 Drawing Figure(s); 8 Drawing Page(s)
LN.CNT 2106
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB This invention provides a ***vaccine*** for the immunization of a vertebrate or invertebrate comprising an avirulent derivative of a pathogenic microbe said derivative being substantially incapable of producing functional adenylate cyclase and cyclic AMP receptor protein. The invention also provides a ***vaccine*** for the immunization of a vertebrate and invertebrate comprising a virulent derivative of a pathogenic microbe said derivative being substantially incapable of producing functional adenylate cyclase and cyclic AMP receptor protein while being capable of expressing a recombinant gene derived from a pathogen of said vertebrate to produce and antigen capable of inducing an immune response in said vertebrate against said pathogen.

L4 ANSWER 25 OF 26 USPATFULL
AN 92:89050 USPATFULL
TI Method of stimulating the immune systems of animals and compositions useful therefor
IN Takayama, Kuni K., Madison, WI, United States
Qureshi, Nilofer, Madison, WI, United States
PA Wisconsin Alumni Research Foundation, Madison, WI, United States (U.S. corporation)
PI US 5158939 19921027
AI US 1990-522446 19900511 (7)
RLI Continuation-in-part of Ser. No. US 1989-383832, filed on 21 Jul 1989, now abandoned And a continuation-in-part of Ser. No. US 1990-467449, filed on 19 Jan 1990, now patented, Pat. No. US 5041427
DT Utility
FS Granted
EXNAM Primary Examiner: Brown, Johnnie R.; Assistant Examiner: White, Everett
LREP Quarles & Brady
CLMN Number of Claims: 6
ECL Exemplary Claim: 1
DRWN No Drawings
LN.CNT 1426
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A method is disclosed for stimulating the immune systems of animals with non-toxic lipid A derivatives. The derivatives include the lipopolysaccharide (LPS) and diphosphoryl lipid A (DPLA) for Rhodopsuedomonas.

L4 ANSWER 26 OF 26 USPATFULL

US 09423546OFP1

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AN 90:81798 USPATFULL
TI Method of inhibiting the activity of leukocyte derived cytokines
IN Mandell, Gerald L., Earlysville, VA, United States
Sullivan, Gail W., Charlottesville, VA, United States
Novick, William J., Lebanon, NJ, United States
PA Hoechst Roussel Pharmaceuticals, Inc., Somerville, NJ, United States (U.S. corporation)
University of Virginia, Charlottesville, VA, United States (U.S. corporation)
PI US 4965271 19901023
AI US 1987-131785 19871211 (7)
RLI Continuation-in-part of Ser. No. US 1986-947905, filed on 31 Dec 1986, now abandoned
DT Utility
FS Granted
EXNAM Primary Examiner: Chaudhuri, Olik; Assistant Examiner: McAvoy, E.
LREP Finnegan, Henderson, Farabow, Garrett & Dunner
CLMN Number of Claims: 14
ECL Exemplary Claim: 1
DRWN 7 Drawing Figure(s); 7 Drawing Page(s)
LN.CNT 807
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB A family of compounds effective in inhibiting interleukin-1 (IL-1) activity, tumor necrosis factor (TNF) activity, and the activity of other leukocyte derived cytokines is comprised of 7-(oxoalkyl) 1,3-dialkyl xanthines of the formula ##STR1## in which R.sub.1 and R.sub.2 are the same or different and are selected from the group consisting of straight-chain or branched alkyl radicals with 2 to 6 carbon atoms, cyclohexyl, alkoxyalkyl and hydroxyalkyl radicals, and A represents a hydrocarbon radical with up to 4 carbon atoms which can be substituted by a methyl group. The inhibition of Il-1, TNF, and other cytokines in mammals is implicated in allerviation of a wide variety of disease conditions.